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MEDICAL ILLUSTRATION IN THE MODERN MEDICAL PROGRAM

ORVILLE A. PARKES*
Augusta

FROM the early crude drawings, made in an attempt to depict what was believed to be the inner workings of man's body, through the excellent illustrations of da Vinci, a man with probably more knowledge of anatomy than the physicians of his day, then to the "Fabrica" of Vesalius, famous for its illustrations attributed to Van Kalkar and without doubt far in advance of anything known up to that time, to the scene of modern present day medical illustration largely developed by Max Brödel at Johns Hopkins and being carried on by his many students throughout the country, one can note the intimate and helpful role played by the medical illustrator. Many others contributed to the development of scientific illustration and the men mentioned are merely the foremost human stepping stones in man's attempt to depict, increase and pass on to others his knowledge of the mysteries of life and the conquering of disease.

In our own day, there are many highly skilled medical illustrators whose sole aim is a desire to assist the medical profession in educating young men in medicine and surgery and to aid in the dissemination of knowledge and research through medical journals, books, movies and other media.

Medical illustration has gained immense momentum in keeping up with the many strides made by medicine and surgery in the past 50 years. The innumerable new technics in surgery have been capably illustrated by the medical artist and photographer, and yet

From the Department of Medical Illustration, Medical College of Georgia.
*Professor of Medical Illustration.

each day heralds new researches and discoveries which must be passed on from man to man, and professor to student usually more accurately and easily understood through the use of visual aids.

It is the purpose of this article to acquaint the practitioner, educator and clinician with the educational background of the present day medical illustrator and how the abilities of this illustrator may best be used in the various fields of medicine.

Max Brödel's course of study for the would-be medical illustrator was extremely simple when compared with present day schools of medical art. The dissecting and drawing of dissected parts was the primary training of the embryo artist, together with drawings of pathological specimens. Sketches in the operating rooms and clinics, and the making of extremely detailed finished drawings were also stressed. Today, medical art students in most schools take essentially the same preclinical work as the medical students, and are graded at that level. For example, in our department at this school, medical art students cover the same courses in Anatomy, Embryology, Histology, Neuro-Anatomy and Pathology with the medical students. In addition, there is the major subject of the technics of medical illustration which is an intensive training in the use of the various media of the artist. Their uses in the clinics and operating rooms and the many problems encountered in illustrating pertinent medical observations are also emphasized in these classes.

Having covered the essential background of the artist, what does he offer the surgeon, researcher and instructor in today's medical program? This can best be expressed by describing the duties, abilities and what is expected of this scientific illustrator.

From the medical educator's standpoint, it is a well accepted fact that lectures and laboratory work can best be assimilated by the student if they are profusely illustrated. The artist and photographer are equipped and trained to provide charts, graphs and drawings in all media to be shown or projected as lantern slides in classrooms. The director of an illustration department should obtain and have projected movies of subjects suggested by the professors of the various preclinical and clinical courses. Three dimensional models of normal anatomical subjects and also pathological specimens should be provided to aid the medical student in understanding normal and pathological conditions. The increase in medical knowledge in the past 25 years has added greatly to the burdens of the medical student in correlating and assimilating the mass of information he must cover in what seems such an inadequate period of time. Illustrated material and movies are assisting in the rapid coverage of these studies. All professors and medical students as well are highly enthusiastic concerning the advantage of well illus-

trated lectures and teaching movies. Thus the medical illustrator, in providing these aids, is of immeasurable value in the education of the medical student.

The research worker is also in need of the services of the medical artist and photographer. The statistical results of investigations must be presented in simple, concise form. Many charts and graphs in the literature are overly long or too complicated to sustain the interest of the reader in their content and are quickly glossed over. The illustrator must advise and assist in simplifying the researcher's material so that its message can be quickly read, and he must also depict accurately the results of the findings. The gross and microscopic studies of diseased tissues and the progress of disease are all well recorded by drawings and photographs, both in black and white and color. Photographic records of tissue growth and cultures are invaluable in noting the progress of research.

Until recent years, the main duties of the medical illustrator was the drawing of pathological specimens and the depicting of surgical procedures, usually for their publication in journals and textbooks of surgery. This demand has not lessened over the years and much time is spent on these problems. Quite often the question is raised as to why photography, with its element of speed and simplicity, is not used to a greater extent for the illustration of surgical practices. This is best answered by pointing out that the camera records everything in the operative field. This field, unless especially prepared, is usually filled with instruments, sponges, hands, etc. It is extremely difficult in many cases to identify the cut tissues, the clamped or ligated vessels and the surrounding anatomy. Points of interest which need emphasis receive no more than the surrounding territory. Blood, photographing very dark, usually obscures many valuable parts of the procedure. Equipment, not only cameras but light sources as well, are usually unwieldy and difficult to maneuver. In contrast, the medical artist by taking a position near the operator records in his sketches the main points of the operation as directed and requested by the surgeon as he continues his operating or examination. On the completion of the operation, the salient points and procedures of interest are discussed by the surgeon and artist, and a plan of how best to illustrate the procedure is worked out. In the completion of the drawings requested, the artist may retract tissues further to more fully show various anatomical areas; the instruments used are kept to a minimum. Gauze, towels and anything which may have obstructed the field during the operation are eliminated or subdued. Only the important phases in the operation are emphasized, resulting in a clear, concise step-by-step record of what occurred. Regardless of the use to which these illustrations

may be put, lantern slides, journal publication or textbooks, the illustrations together with the author's comments quickly inform the reader as to the routine followed.

The examination of the cavities of the body through cystoscopes, bronchoscopes, gastroscopes, and other procedures, the findings therein and the progress of disease, can be well illustrated and passed on to others through the services of the illustrator. In this field, the camera is a valuable assistant in the recording of conditions observed. Much progress has been made in recent years to perfect cameras for this purpose.

In many cases, especially in the field of plastic surgery, it is desired to record the improvement of surgical repair. Plaster and wax models of conditions before and after operation assist in pointing out the degree of improvement obtained. Here again the teaching value of these products cannot be overestimated. Many plastic surgeons plan the amount of correction necessary directly on the plaster cast made of the patient before operation. For example, the amount of bone to be removed in a rhinoplasty can be quickly calculated and the final result visualized by cutting one side of the plaster nose to a desired contour. These casts are often referred to by the surgeon in the operating room, and also assist in acquainting the patient with the result he or she may expect.

The use of facial prostretics for disfigurements due to trauma or disease are now widely used. The improvement in materials available for these appliances and the skill of the artist in their making, has enabled the patient to lead a more normal life until surgery is employed to correct the defect, or even as permanent aids in covering the disfigurement. Loss of the nose, an ear or an eye can result in personality changes and depression which can largely be avoided through the use of a prosthesis. To many patients, the wearing of such aids becomes routine, much like glasses or false teeth. As previously mentioned, plastic materials have been developed, which in their finished form, have the appearance and feeling of normal tissue, and when matched in color to the patient's skin are scarcely noticeable.

The dissemination of knowledge within the profession of medicine has been accomplished in large part through the scientific exhibits presented at all major medical meetings each year. The largest and most diversified of course has been that at the annual sessions of the American Medical Association. These were largely presented in a rather haphazard manner in early years, but have been developed into quite lavish and intricate displays in recent times. It is not only the ambition of the doctor presenting the exhibit but

of the artist preparing it as well that it will win one of the awards annually presented. Illustrators attending these meetings for the purpose of installing the exhibit and of obtaining new ideas for use in future years, examine with minute care the work of their contemporaries. An exhibit does offer a unique method for the presentation of research work from year to year; however, in many cases these exhibits seen by a small fraction of the profession may be filed away only to gather dust after their initial presentation. It would be a very excellent program if there was an agency or individual to assume the distribution of the "cream of the crop" of these exhibits from medical school to medical school so that people other than those attending meetings could also view these productions which are otherwise doomed to the storage room or destruction.

Movies are being used widely in teaching programs and for the purpose of acquainting the medical profession with new technics in surgery and medicine. There is no question as to the value of these films for the rapid assimilation of new material. Particularly valuable are films depicting the various stages of dissection in conjunction with the anatomical courses. Before proceeding with the dissection of a particular area of the body, the student is enabled to observe the proper procedure of dissection and the structures he will encounter. Films made in the operating rooms give the instructor an opportunity to pass on to students and contemporaries his own technics of surgical repair. This latter process will no doubt be largely replaced by television projection to classrooms direct from the operating theater, thereby enabling a larger group to observe more satisfactorily the various surgical procedures. This new medium will no doubt be the responsibility of the medical illustration department.

It can be seen from the description of the various routine duties of an illustrator, the intimate and helpful role he occupies in the modern medical program. To quote a contemporary, Professor Tom Jones of the University of Illinois School of Medicine, "The field of the medical illustrator is no longer an appendage to, but an integrated and indispensable part of the pattern of medical education."

In summary: The present day scientific illustrator should be prepared to provide a wide variety of medical illustrations. He must design, develop and guide the production of exhibits, motion pictures and three dimensional models. These reflect his training and capabilities, and should meet the needs of present day medicine. Tom Jones further said, "Not only should the scientific illustrator have a knowledge of anatomy of the body equal to, if not beyond that of the physician—but also he must know something of the

anatomy of understanding as well. For the psychological basis of visual education, as well as the limitations and advantages of the various media employed are his concern and responsibility."

Much has been accomplished to improve the training and professional status of the medical artist by the Association of Medical Illustrators which was chartered in 1944. The high quality of standards laid down and certain basic qualifications fostered by this association for schools of medical art will result in a more complete coverage of preclinical subjects and art studies.

The trend toward the awarding of both Master of Science and Doctor of Philosophy degrees to properly qualified students will further enhance the professional standing of the future medical illustrator. At the present time, only Southwestern Medical College and our school at this institution award degrees, but others are certain to follow.

Even as the medical student faces the ever enlarging expanse of knowledge he must absorb, so too must the medical illustrator keep pace with his knowledge and assistance to provide the needs of visual education in today's and the future program of medical education.

A LYMPHATIC DEFECT IN HYDROCELE

J. Robert Rinker, M.D.*
Lane Allen, M.D.**
Augusta

The more theoretical aspects of hydrocele have hardly been considered in the literature. There are perhaps two reasons for this: first, obliteration or excision of the sac constitutes adequate treatment; second, no animals except man show the anatomical separation of sac and peritoneal cavity and hence animal experimentation is not possible.

This work was prompted by an anatomical study by one of us (Allen, 1943) on the normal mechanism of drainage of the sac in man. It was discovered that the parietal tunica vaginalis of man possesses a lymphatic plexus comparable to the subserous plexuses of the diaphragm and intercostal pleura and that the common laboratory animals, whose vaginal processes remain patent throughout life, do not show lymphatic plexuses in the parietal tunica vaginalis.

Material and Methods

The tunica vaginalis was searched for the presence or absence of lymphatic plexuses in 4 instances. Two different methods were employed: fine needle preoperative injection of india ink directly into the sac and routine histological sectioning.

Controls. Two hours prior to castration of a 55 year old male for carcinoma of the prostate, 5 cc. of 50 per cent Higgins india ink in normal saline were injected into the two sacs. The sacs with the contained testes were removed entire at operation and fixed in 10 per cent formalin.

Congenital hydrocele. This specimen consisted of the stripped tunica vaginalis from a 12 year old boy. The specimen was fixed in 10 per cent formalin, sectioned and stained with hematoxylin and eosin.

Hydrocele, acquired, idiopathic. This specimen consisted of the stripped tunica vaginalis of a male of 45 years of age. Two hours before operation the sac was aspirated and 10 cc. of ink saline suspension were reinjected. The specimen was fixed in 10 per cent formalin.

Hydrocele, acquired, idiopathic. The specimen consisted of the

From the Department of Urology and the Department of Gross Anatomy, Medical College of Georgia.
*Professor of Urology.
**Professor of Gross Anatomy.

stripped tunica vaginalis of a male of 48 years of age. The specimen was fixed in 10 per cent formalin, sectioned and stained with hematoxylin and eosin.

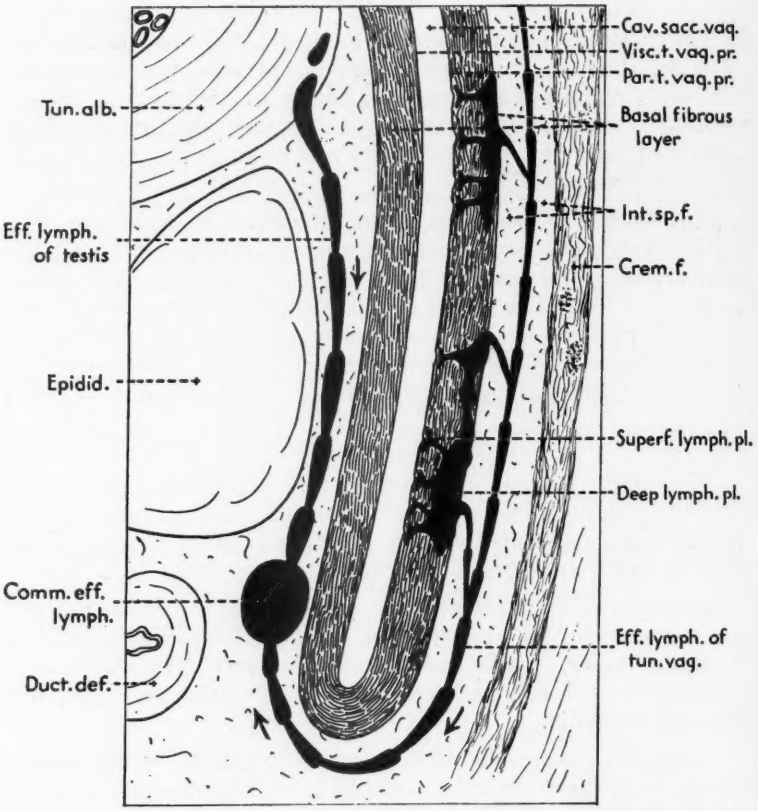

Fig. 1. Section of testis and saccus vaginalis showing deep and superficial lymphatic plexuses which occur in the basal fibrous layer of the parietal tunica vaginalis propria. The efferent lymphatics of the tunica vaginalis course around the parietal tunica vaginalis propria from the medial to the lateral side and enter a common efferent lymphatic which also receives efferent lymphatics of the testis.

Observation and Discussion

The absorptive mechanism in the normal sac. *Figures 1, 2, 3, 4, and 5 show the lymphatic drainage of the normal sac. These lymphatics occur in scattered plexuses lying within the basal fibrous

*Reprinted from the Anatomical Record with permission of the Wistar Institute.

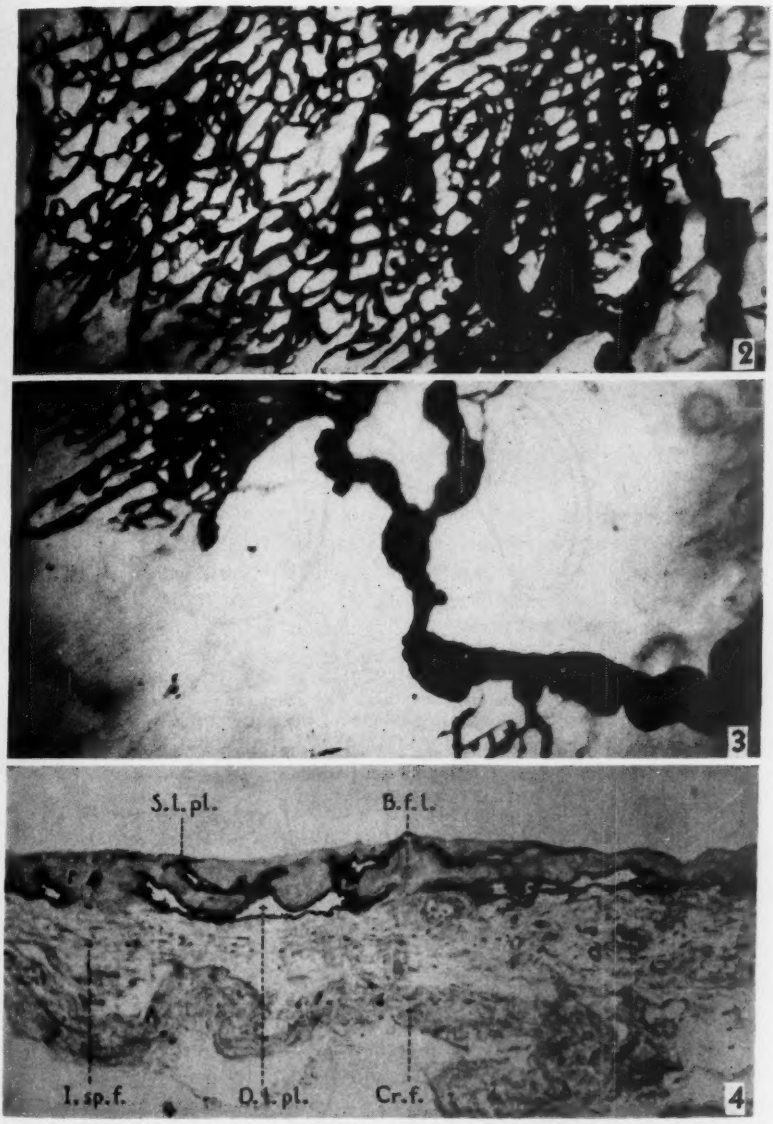

Plate 1. Explanation of Figures. Fig. 2. A whole mount showing superficial and deep plexuses of parietal tunica vaginalis propria. India ink injection. This plexus is 5 mm. in diameter. Fig. 3. A whole mount showing a large efferent lymphatic channel draining three subserous "patches." India ink injection. Fig. 4. A subserous lymphatic plexus in section. India ink injection. Note that both the superficial and deep plexuses are confined to the basal fibrous layer. S. l. pl., superficial lymphatic plexus; D. l. pl., deep lymphatic plexus; B. f. l., basal fibrous layer; l. s. f., internal spermatic fascia; Cr. f., cremaster fascia.

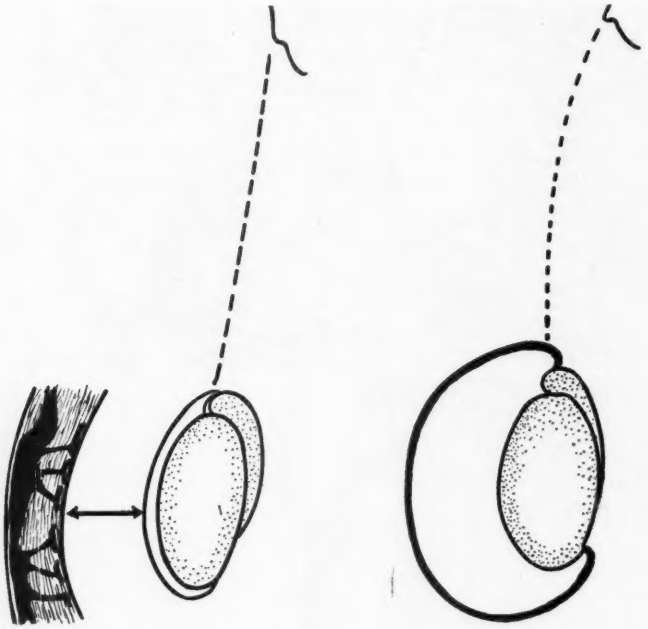

Fig. 5 Fig. 6

Fig. 5. Normal parietal tunica vaginalis from 55 year old male, sac injected with india ink 2 hours before castration. The offset shows the absorption of ink by the lymphatic plexuses of the parietal tunic.

Fig. 6. Hydrocele. The parietal tunica vaginalis is thickened and scarred with lymphatics obliterated.

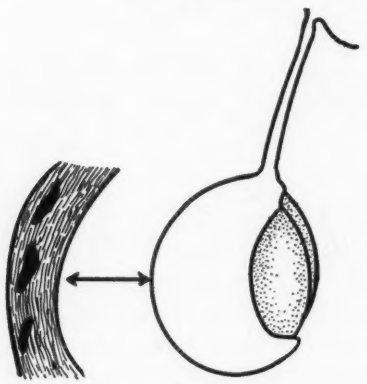

Fig. 7

Fig. 7. Congenital hydrocele. The parietal tunica vaginalis is thickened and the normal subserous lymphatic plexus is absent. The lymphatics which are present are far removed from the mesothelial lining and are either remnants of the deep plexus or represent a secondary lymphatic invasion.

layer of the parietal tunica vaginalis propria. Each plexus consists of a deep and superficial portion, the superficial plexus lying in direct contact with mesothelial lining of the sac. Although there are extensive lymphatic plexuses lying within the tunica albuginea testis, these vessels constitute the efferent drainage of the testis and do not participate in drainage of the sac. Lymphatic absorption from the sacs and flow along the efferent channels is essentially similar to lymphatic absorption from other serous cavities (MacCallum, 1903; Allen and Vogt, 1937) and is probably effected by the smooth muscle of the dartos tunic and Muller's muscle. The latter consists of smooth muscle fibers which originate in the hilum of the testis and insert into the basal fibrous layer of the sac.

The normal control (fig. 5) showed extensive filling of the subserous lymphatics of the sac with india ink. These vessels filled with ink were observable with the naked eye. In none of the other specimens (figs. 6 and 7) were the characteristic subserous lymphatics observed. In one specimen (congenital hydrocele, fig. 7) a few deep lymphatics were seen in sections. These could be a secondary invasion of the sac or remnants of the original plexus largely obliterated by the general fibrosis characteristic of hydrocele sacs. In either event from what is known of the normal physiology of subserous lymphatics these outlying lymphatics could not take part in absorption from the sac. Accordingly it may be concluded that there is a lymphatic defect in hydrocele. It is of theoretical interest in this connection that lower animals which exhibit a patent processus vaginalis throughout life (Symington, 1914) likewise exhibit a lymphatic deficiency in the tunica propria.

In studies on the absorption of the tunica vaginalis, Huggins and Entz found that phenolsulphonphthalein was absorbed by the normal tunica vaginalis appearing in the urine in 40 to 60 minutes but when injected into idiopathic hydrocele none appeared in the urine in 24 hours, indicating a defect in the mechanism of absorption.

Summary

The above studies lead us to believe that inadequate absorption of the fluid through the lymphatics of the processus vaginalis is the basic cause in both congenital and idiopathic hydrocele, though the predisposing factors in the two types are somewhat different. Congenital hydrocele occurs when the lymphatics of the tunica vaginalis are not adequately developed to remove the fluid after the closing of the communication between the processus vaginalis and the peritoneal cavity. Timing of the closure of the patent processus vaginalis with the development of the lymphatics in this structure may be the deciding factor as to whether or not a congenital hydrocele

will be present. The descent of the testicle, development of the lymphatics to a functioning state in the processus vaginalis, and closing of the communication with the peritoneal cavity are late processes both phylogenetically and ontogenetically. Hydroceles which are present at birth and can not be erupted back into the peritoneal cavity cure spontaneously within the first year of life, in many cases. This suggests that the lymphatics were not adequately developed at the time of birth and complete their development after birth. Expectant treatment is rational in these cases. In chronic or idiopathic hydrocele permanent damage to the lymphatics appears to have taken place. Cure of the hydrocele is effected by surgery or sclerosing solution because the secreting membrane is removed or rendered incapable of this function and the space is obliterated so there is no place for the fluid to collect. Whether the acquired hydrocele is transitory (acute) or permanent would depend on the degree of irreversible damage to the lymphatics in the tunica vaginalis.

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DIVERTICULUM OF THE URETHRA IN THE FEMALE

J. Robert Rinker, M.D.*

Augusta

Diverticulum of the urethra in the female is a lesion which is frequently overlooked in the search for the cause of dysuria, because physicians do not often consider it as a possible cause of lower urinary tract symptoms. If only inspection and palpation are relied on to make the diagnosis, the lesion will be discovered in less than half of the patients in which it exists, according to the experience of the writer.

For the purpose of diagnosis we can divide the patients who have this lesion into two groups, according to the signs they present of the existing pathology. In one group, a swelling may be seen protruding into the vagina or vaginal vestibule or palpated through the anterior wall of the vagina anywhere along the course of the urethra. Pressure on the diverticulum with the palpating finger may cause it to empty into the urethra and a drainage of pus or infected urine will appear at the urethral orifice. In this group the lesion is easily diagnosed and the abnormality frequently noticed by the patient or nurse during a routine catheterization or other examination. In the other group, the diverticulum will not be found unless an examination of the urethra is directed at discovering the lesion. In these cases it may be too small to detect on inspection or palpation or it may arise high on the lateral wall of the urethra and occupy a space lateral to the urethra, consequently, less evident than those cases where it is located nearer the midline. Careful examination of the urethra with the McCarthy Panendoscope with or without palpation of the diverticulum may disclose the opening which may be as high as 2 o'clock, and as far proximal as the vesical sphincter. Further evidence as to the size may be gained by passing a urethral catheter into the opening of the diverticulum or by urethragram.

Obtaining a negative catheterized specimen of the patient's bladder urine may disarm the physician, causing him to minimize the patient's complaints. While a catheterized urine specimen for diagnostic purposes is always desirable in the female, one may, in these cases, bypass the opening of the diverticulum which contains pus and obtain a negative bladder urine.

In 5 of the 13 cases studied, the diverticulum was of the large type that could be seen or diagnosed by palpation, and 8 were in

*Professor of Urology.

From the Department of Urology, Medical College of Georgia.

the group which would have been missed had the diagnosis not been made by urethrascopic examination.

The size of the diverticulum seemed to bear little relationship to the degree of the patient's discomfort and symptoms. In some of the larger diverticula the presence of the mass seemed to be the only symptom, while in the smaller ones the patient invariably came for treatment because of burning in the urethra during or after urination. In one patient the pain was excruciating for about 10 minutes after voiding due to an associated urethritis secondary to the infected diverticulum. Leakage of urine after voiding as the diverticulum emptied was a frequent sign and annoyance to the patient.

Complications may be associated with the diverticulum. In one patient the ostium became sealed due to chronic inflammation and an acute exacerbation of diverticulitis with symptoms followed. In another case the same thing apparently occurred and the resulting infected diverticulum ruptured and drained into the vagina after burrowing through the anterior vaginal wall, resulting in a fistula. After this drainage of the diverticulum, the ostrum in the urethra became patent and on voiding the diverticulum filled and then emptied through the small fistulous opening into the vagina. One large diverticulum contained a calculus.

The treatment is surgical eradication. The large diverticula and four of the smaller ones were removed by open surgery through an incision in the anterior wall of the vagina. The opening in the urethra at the site of excision was sutured and the vaginal wound closed. A Foley bag catheter was left inlying for about six days and a vaginal pack left in place for three days. The wounds have healed in all cases without fistula formation. In 4 of the small diverticula, cure was achieved by removing the separating wall of the urethra and diverticulum with the diathermic knife through the Panendoscope, converting the remaining portion of the small diverticulum into a part of the lumen of the urethra.

As to whether the lesion is acquired or due to congenital predisposition is of academic interest. One of the above patients gave a history which suggested the presence of an abscess that had ruptured into the urethra and the diverticulum was possibly the result.

Discussion

The trend of the recent literature regarding this subject indicates that more patients having diverticula of the urethra are being discovered as physicians become more aware of the possible existence of the lesion. Surgical eradication of the diverticulum is the treatment of choice. The results in the treatment of these patients has been very satisfactory.

PRIMARY RETICULUM CELL SARCOMA OF THE LUNG ARISING IN THE WALL OF PULMONARY CYST

A Case Report

HERBERT T. RANSDELL, JR., M.D.*
ALBERT W. BAILEY, M.D.**
ROBERT G. ELLISON, M.D.***
Augusta

PRIMARY sarcoma of the lung is a relatively rare condition. Lenk in 1929 (as quoted by Baum[1]) estimated that only .009 to .02 per cent of all autopsies show sarcoma of the lung and quoted Boschowsky as summarizing the literature up to 1912 and finding only 63 cases in the preceding 55 years. No doubt, however, many of these cases would today be classed as small cell or oat cell carcinoma. Adler in 1913 as quoted by Pilot[2] stated he had not observed a single case and found 94 cases of sarcoma reported in the literature but maintained that most of them fell into the category of round cell carcinoma. Stevens[3] in 1912 stated that only four primary sarcomas of the lung were found in 9,246 autopsies at the Breslau Pathological Institute, and Mallory[4] in 1936 reported seeing only one case of primary lung sarcoma in 8,000 autopsies in his experience. Ball[5] in 1931, reviewing the English, French and German literature from 1900 to 1931, and using relatively rigid criteria in selection of cases, found 13 cases and added 1 of his own. Rosenblaum and Gasul[6] reviewed the pediatric literature in 1931 and found 13 cases in infants and children, one of which was included in Ball's review, and added 1 of their own. In 1938 Baum reported a case of primary sarcoma of the right main stem bronchus treated by x-ray and added 8 cases of primary lung sarcoma not included in Ball's review. Other case reports found in the English literature since 1938 include 3 of the Massachusetts General Hospital Clinical pathological conferences,[7,8,9] 2 cases by Gray,[10] and one each by Pollak,[11] Carlucci,[12] Spatt,[13] and Hochberg.[14]

In a review of the literature, we have been able to find only 2 case reports of primary sarcoma of the lung originating in the wall of a pulmonary cyst. Giraud[15] described a case of primary reticulum cell sarcoma arising in the wall of a pulmonary cyst in a 3½ year

From the Departments of Thoracic Surgery and Pathology, Medical College of Georgia.
*Resident, Thoracic Surgery.
**Resident, Pathology.
***Assistant Professor of Thoracic Surgery.

old male infant, and Behrend[16] reported surgical removal of a fibrosarcoma arising in the wall of a bronchogenic cyst in a 25 year old man with death of the patient 8 months later due to mediastinal metastases.

The following case of a sarcoma developing in the wall of a pulmonary cyst is thought to be the third such case reported.

A 37 year old white male was admitted to the University Hospital on Feb. 1, 1951, complaining of "soreness in my chest" and "spitting up blood." About five months prior to his admission he began to note vague intermittent soreness of gradually increasing severity in the right anterior mid chest region. During the five months discomfort had gradually spread inferiorly to the right costal margin anterolaterally and to the low subscapular region posteriorly. A routine Public Health 70 mm. survey chest film taken at the patient's place of employment Nov. 26, 1950, followed by a 14 by 17 film (fig. 1) November

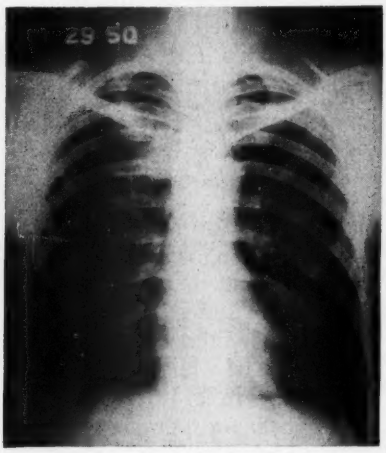

Fig. 1. Posteroanterior chest film. November 29, 1950.

29, revealed a small, ill-defined mass projecting from the right upper mediastinum at the level of the first interspace anteriorly and a cystic appearance of the right upper lung field. This was reported by a radiologist as suggestive of bronchogenic carcinoma with obstructive emphysema, and further diagnostic studies advised. For three months prior to admission he had had mild to severe night sweats two or three times weekly. He had also noticed an occasional slight expiratory wheeze, not relieved by cough, in the upper right parasternal region for the preceding few weeks. For several years he had had a chronic dry "cigarette cough." Two weeks prior to admission he developed a rather severe upper respiratory infection, shortness of breath when lying on his right side, and marked increase in his cough which then became productive of small amounts of thin, mucoid, occasionally slightly blood streaked sputum. Following administration of aureomycin prescribed by his physician, this infection gradually subsided over a period of 7 to 10 days, cough improved, sputum

decreased and hemoptysis ceased. There had been a slight decrease in appetite for the past year and a weight loss of 12 to 15 pounds in the last six months. He had noted no particular langour or generalized malaise.

Past medical history revealed good health except for an attack of "typhus fever" of about four weeks' duration seven years previously. Childhood diseases consisted of uncomplicated whooping cough, and pneumonia. Two years prior to admission he sustained an injury to his right chest, following which he experienced severe pain for several days. He had smoked one package of cigarettes every two to three days all his life, and there was no history of inhalation or ingestion of gases or drugs. He had worked in a textile mill for the past 18 months and prior to that had been a farmer.

Physical examination revealed a well developed, slightly malnourished, 37 year old white male of slender, athletic build who appeared chronically ill but in no apparent discomfort. There was evidence of recent weight loss. Poor

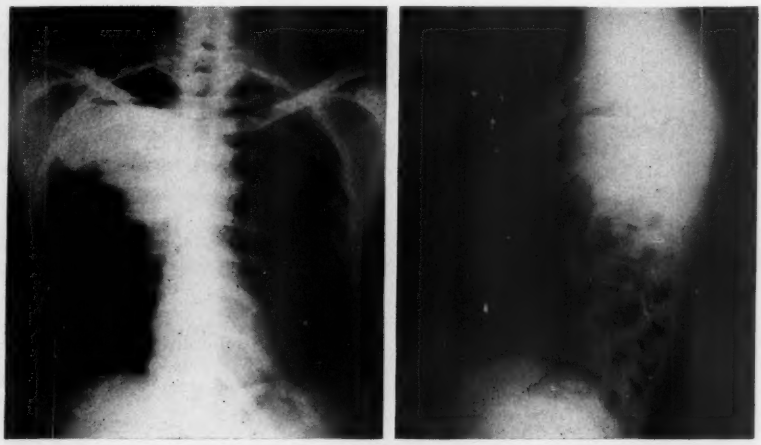

Fig. 2 a and b. Posteroanterior and lateral admission chest films.

oral hygiene with moderately severe pyorrhea alveolaris and foul breath was present. The trachea was in the midline, and there was no significant lymphadenopathy. Chest examination revealed equal and regular expansion and no abnormalities of the chest wall except for slight prominence of the veins over the anterior chest wall and arms. There was dullness to percussion over the upper third of the right lung particularly anteriorly, with definite increase in vocal fremitus and moderate depression of breath sounds over the upper half of the right lung particularly subclavicularly. Whispered pectoriloquy was present over the right supraclavicular area. No rales or rhonchi were heard. The left lung and lower portion of the right lung were normal. The remainder of the physical examination was normal. There was no clubbing of the digits.

X-rays of the chest (figs. 2a and 2b) on admission to the hospital revealed marked enlargement of the previously noted hilar mass and the development of a fluid level in the cystic area.

Admission laboratory studies showed a red blood cell count of 2,920,000 with 9.4 Gm. of hemoglobin and a white cell count of 16,150 with 89 neutrophils, 7 lymphocytes and 4 monocytes. Urine was essentially normal. Blood chemistry determinations showed normal chlorides, N.P.N. and sugar and a total protein of 7.2 Gm. with 3 Gm. of albumin and 4.2 Gm. globulin. Sputum was negative for acid fast organisms.

Venous pressures in the right arm were normal. Bronchoscopy revealed an essentially normal tree. Bronchial washings showed much mucus, leukocytes, and desquamated epithelial cells and occasional clumps of small, pyknotic cells of questionable, but not diagnostic, nature. The conclusion was probable infected pulmonary cyst with carcinoma to be ruled out.

On admission the patient had a temperature of 101 and, while being prepared for surgery with multiple transfusions, he ran a moderately severe septic temperature which failed to respond to chemotherapy. Although bronchogenic carcinoma could not be ruled out, a tentative diagnosis of infected

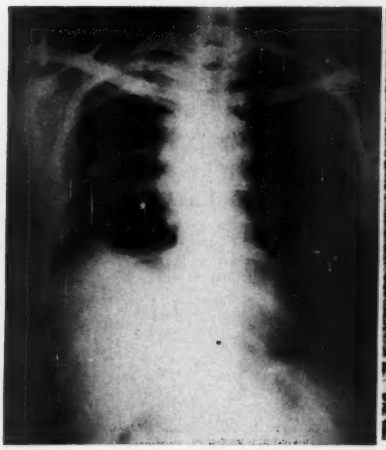

Fig. 3. Posteroanterior chest film 10 days postoperative.

Fig. 4. Low power photomicrograph of tumor and adjacent lung. Superiorly is seen the infected necrotic tumor (A) bordered inferiorly by a shell of viable neoplastic cells (B). Subjacently is compressed lung parenchyma with fibrosis and reversionary metamorphosis of the alveolar wall (C). (X 50.)

pulmonary cyst was made and exploration done on Feb. 9, 1951. Exploration revealed the upper two-thirds of the upper lobe rigidly adherent over the apex down to the level of the fourth interspace posteriorly, the third interspace laterally and the second interspace anteriorly. The apical and anterior segments of the upper lobe were replaced by a grapefruit sized, thick walled, tense, fluid filled cyst and the posterior segment was consolidated apparently by chronic infection. The middle and lower lobes appeared normal. The upper lobe was mobilized by extrapleural dissection. The consolidated posterior segment was rigidly adherent to the superior vena cava. Because of danger of injuring the vena cava, a thin portion of apparently chronically infected lung

tissue, measuring about ½ cm. in thickness by 1 to 2 cm. in width, by 4 cm. in length, was left attached. After mobilization of the lobe there were no nodes palpated in the hilum. It was thought this was an infected cyst with adjacent pneumonitis and an upper lobectomy was done by individual ligation technic. The chest was closed in layers with interrupted cotton leaving two No. 32 rectal tubes in the pleural space for drainage. The postoperative course was uneventful. Postoperative x-rays revealed good expansion of the middle and lower lobes to obliterate the pleural space (fig. 3), but fluoroscopy revealed paralysis of the right diaphragm. Apparently the phrenic nerve had been injured in the process of freeing the mass from the superior vena cava.

Pathology report was as follows: "Reticulum cell sarcoma of the lung." The gross specimen consists of the upper lobe of the right lung. There is a loculated cyst 7 cm. in diameter which replaces the apical portion of the lobe and which is filled with sero-sanguinous fluid; this cyst balloons the visceral pleura somewhat on the lateral, anterolateral, and posterolateral aspects. The

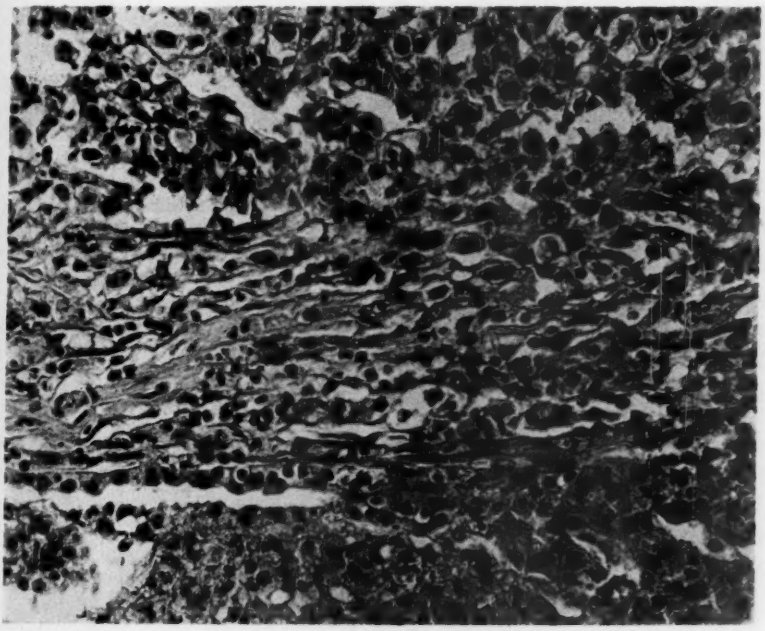

Fig. 5. High power photomicrograph of tumor and adjacent lung. Viable reticulum cell sarcoma in the superior aspect of the photomicrograph with subjacent compressed lung characterized by fibrosis and chronic pneumonitis.

wall of the cyst consists of moderately heavy fibrous connective tissue. Inferiorly and in part medially to the cyst is a necrotic tumor mass 7 by 6 cm. which extends to the medial line of excision at the groove of the superior vena cava superior to the right main stem bronchus. The center of the approximately spherical neoplastic mass lies well within the lung and invades the fibrous wall of the cyst at its mid medial inferior portion. The tumor extends

to the anterior and posterior medial margins in the lower portions of the upper half of the lobe and is separated from the pleura at these sites by a fibrous wall. Only a narrow shell of the neoplasm remains viable around the periphery of the necrotic tumor (fig. 4). The subjacent portions of the lobe are compressed by the neoplasm, and here there is chronic pneumonitis characterized by organizing exudate and fibrosis. Along the posterolateral border below the neoplasm there are four small bronchial cysts, each filled with fluid hemor-

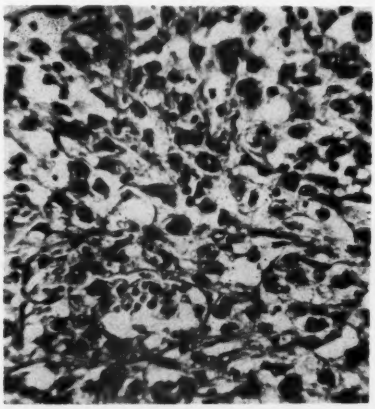

Fig. 6. High power photomicrograph of tumor. Pleomorphism with anisocytosis and anisokaryosis is noted as well as anastomatic processes between cells. The neoplastic cells have large, vesicular, hyperchromatic nuclei with prominent nucleoli and form support for thin walled capillaries.

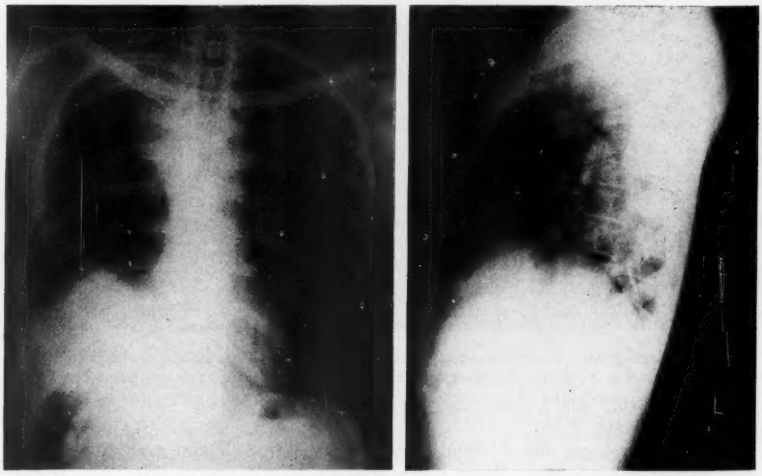

Fig. 7 a and b. Posteroanterior and lateral chest films 3 months postoperatively and 1 month following completion of x-ray therapy.

rhagic contents. The largest measures 2 by 1.5 cm. The cells of the viable neoplasm suggest origin from the septal reticulum (figs. 5 and 6). The cells

are large generally with solitary nuclei, but occasionally binucleated and multinucleated; there is pleomorphism as well as anisocytosis and anisokaryosis. The nuclei are vesicular and hyperchromatic with prominent chromatin which is at times arranged primarily circumnuclearly; there are prominent nucleoli. While there are anastomotic processes between cells there is also deposition of the reticulum. The neoplastic cells form the support for thin walled capillaries. There is a generous leukocytic infiltrate throughout the necrotic neoplasm. There is a striking resemblance between the tumor cells and the macrophages in the subjacent pneumonitis which, with the exception of nuclear anaplasia, is most striking. The epithelium of the alveolar walls proximate to the fibrous tissue in the compressed portions of the lung has undergone reversionary metamorphosis (fig. 5).

The appearance of this tumor leads us to the diagnosis of a reticulum cell sarcoma which well might have its origin from septal cells. The tumor is well within the lung and has escaped the confines of the visceral pleura over an area of approximately 4.5 cm. in diameter at the site of the pre-existing fossa of the superior vena cava. That the neoplasm might have arisen in the medial inferior wall of the apically placed congenital cyst is strongly suggested from the gross appearance and localization of the center of the neoplastic mass in relation to the loculated apically placed cyst.

Since pathological examination of the specimen revealed the sarcoma extending to the line of excision of the mass from the superior vena cava, it was felt the patient should be given the benefit of x-ray therapy. He received a tumor dose of 4,500 R to his right superior mediastinum through multiple ports over a period of two months. X-rays of chest on May 7, 1951 (fig. 7) revealed the presence of a mass in the right superior mediastinum. It was thought that this was probably due to progressive growth of the neoplastic tissue. The patient was last seen on May 12, 1951. He was asymptomatic and anxious to return to work.

SUMMARY

1. A brief review of the literature in reference to primary sarcoma of the lung is given.

2. A case of primary sarcoma apparently arising in the wall of a congenital pulmonary cyst is presented. This is believed to be the third such case reported in the literature.

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PRIMARY CARCINOMA OF THE FALLOPIAN TUBE

Report of Two Cases

G. L. Calk, M.D.*
C. M. Phillips, M.D.**
Augusta

THE subject of primary carcinoma of the fallopian tube has been extensively reviewed by several authors and cases collected from the literature have been recently analyzed by Olesen and Albeck[1] in 1949 and Hu, Taymor and Hertig[2] in 1950. The former authors were able to collect 479 cases from the literature and added 1 of their own. The latter authors reviewed the literature and added 12 cases. Since these reports there have been 2 cases reported by Johnson,[3] 1 case by Cruttenden and Taylor,[4] 1 case by Stern and Hanley,[5] 1 case by Neiman and Russ[6] and the 2 cases herein reported bringing the total to approximately 499 cases. A report of 2 cases follows:

Case 1. E. J., a 53 year old colored female, was admitted to the Macon Hospital on Oct. 26, 1950, with the chief complaints of lower abdominal cramping and considerable pressure in the epigastrium. The present illness began 9 months prior to admission when she noticed discomfort in the epigastrium and slight abdominal swelling, both of which had become progressively worse. The menstrual history revealed an onset at 13 years of age with an interval of 28 to 30 days and duration of four to five days. The periods were characterized by slight cramping in the lower abdomen until the flow was established. Spontaneous menopause had occurred at the age of 41 years. There had been no vaginal bleeding since the cessation of menses but she occasionally had been troubled by an unusually irritating vaginal discharge which was relieved by douches. There was no history of pregnancy. The past and family histories were noncontributory.

Physical examination revealed a blood pressure of 130/98, pulse rate of 76 per minute, respiratory rate of 18 per minute, temperature of 98.8 F. and weight of 75 Kg. with no recent history of weight loss. The abdomen was slightly distended. There was no tenderness or rigidity. A firm nodular mass was palpable in the right lower abdomen. The external genitalia were within normal limits. The introitus was marital in type. The vaginal vault was slightly atrophic and clean. The cervix was small and nulliparious in type. The abdominal tumor was found to be arising from the pelvis and consisted of a bilobular mass, the two lobes being estimated at 18 and 8 cm. in diameter respectively. The remainder of the physical examination was essentially negative.

The laboratory data were as follows: Vaginal and cervical films stained by the method of Papanicolaou revealed no malignant exfoliated cells. The

From the Departments of Obstetrics and Gynecology and Pathology, Medical College of Georgia.
*Resident, Obstetrics and Gynecology.
**Assistant Professor of Pathology.

catheterized urine specimen was negative. Examination of the blood revealed 9.9 Gm. of hemoglobin, red blood count of 3,370,000 and white blood count of 7,750 with 57 per cent polymorphonuclear neutrophilic leukocytes, 42 per cent lymphocytes and 1 per cent eosinophils.

The clinical impression was fibromyomata uteri. A whole blood transfusion was given in preparation for surgery.

Under general anesthesia on the morning following admission an exploration of the peritoneal cavity through a suprapubic paramedian incision revealed a retort-shaped tube attached to an ovarian cyst on the right side. The tubo-ovarian mass was mobile. The uterus and left ovary were atrophic. The remainder of the abdominal viscera were in the usual anatomical relationships and were not unusual. The right tubo-ovarian mass, left tube and ovary and uterus were excised en masse.

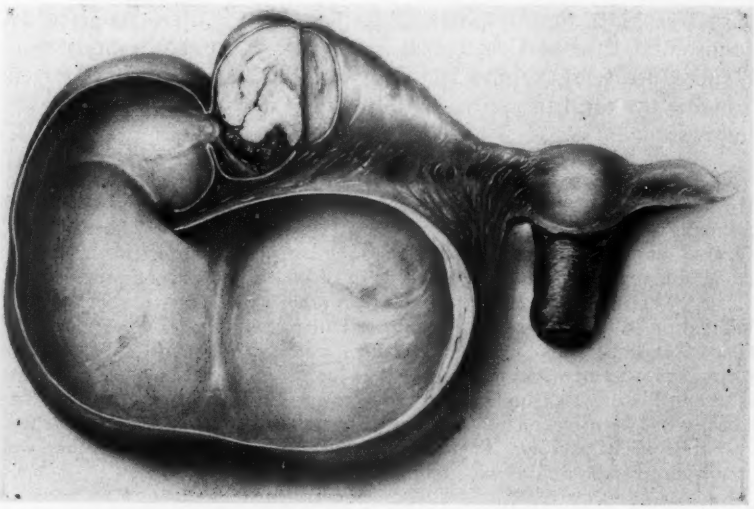

Fig. 1. Primary carcinoma of fallopian tube in a hydro-ovarian-salpinx (case 1).

Pathological examination revealed a papillary adenocarcinoma of the distal half of the right fallopian tube which measured 3 cm. in diameter and 9 cm. in length (fig. 1). The neoplasm extended to within 1.3 cm. of the fimbriated end which opened into an ovarian cyst without proper lining to form a hydro-ovarian salpinx. Most of the neoplastic cells were moderate in size; an occasional tumor giant cell was present. The cytoplasm was small in amount. The nuclei were large, slightly pleomorphic and slightly vesicular. Numerous mitotic figures were present. Many of the neoplastic cells form atypical glands which were thrown up into papillary folds with delicate fibrous cores. In some areas the cells were growing in sheets and masses of glands with a small amount of supportive stroma (figs. 2 and 3). There was an exudate consisting chiefly of polymorphonuclear neutrophilic leukocytes and a few lipoid-laden macrophages between the papillary processes of the neoplasm. There was a chronic inflammatory cell infiltrate consisting largely of plasma cells and

lymphocytes with an occasional focus of pigment-laden macrophages in the wall of the tube. Serosal adhesions bound the tube to the ovarian cyst which measured 20 by 15 cm. A small amount of old blood clot and fibrin was attached to the inner lining of the cyst.

Serosal fibrous adhesions were attached to the body of the uterus which included two interstitial fibromyomas measuring 1.5 and 0.5 cm. in diameter respectively. The endometrium was atrophic. There was an occasional focus of residual cystic glandular hyperplasia of the endometrium. The external os of the atrophic cervix was pinpoint in size and nulliparous in type. Chronic cervicitis with inflammatory cell infiltrate consisting largely of lymphocytes and plasma cells of the portio and junctional endocervix was present. Focal areas of squamous metaplasia were noted.

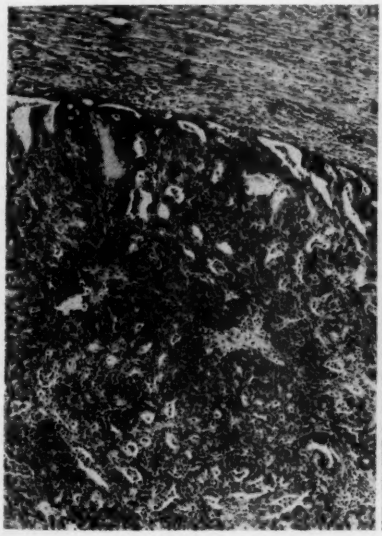

Fig. 2. Papillary adenocarcinoma. Papillary projections near the fimbriated end of the tube.

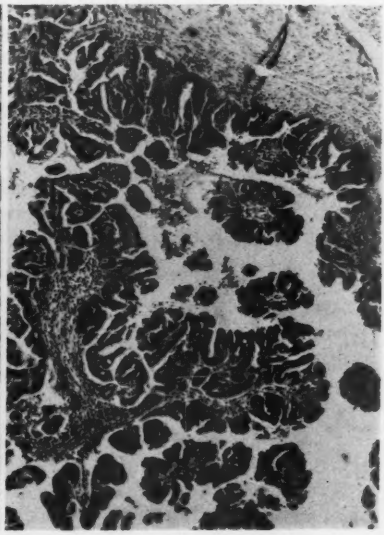

Fig. 3. Papillary adenocarcinoma. An area of solid adenocarcinoma including a portion of the wall of the tube.

There was residual salpingitis of the attached left tube, fibrosis of the wall and the fimbriated end was sealed; the lumen was dilated to a diameter of 1 cm. at the fimbriated end by clear fluid (hydrosalpinx). The attached left ovary was atrophic. There were cortical adhesions with a scattered infiltrate of pigment-laden macrophages and inflammatory cells.

The postoperative course was uneventful. The patient was discharged on the sixth hospital day and followed in the outpatient department at regular intervals. At the last visit, six months following surgery, no masses were palpable on pelvic examination and the chest roentgenogram was negative.

CASE 2. P. C., a 42 year old married nulliparous colored female, was admitted to the University Hospital on Aug. 3, 1935, with a chief complaint of irregular menstruation. The present illness began two years prior to admission

when the patient complained of a slight vaginal discharge and pain in both lower quadrants. During the year prior to admission she had menstruated only three times, the last beginning three days previous to and being more profuse at the time of admission. She also complained of backache and a "pulling down" sensation in the pelvis. Menstrual history revealed an onset at 14 years of age with a regular interval of 28 days and of four to five days' duration. The flow had always been scanty in amount until the onset of the present illness. A history of gonorrhea was related one year following marriage. The past history was otherwise essentially negative.

The physical examination revealed a blood pressure of 105/70, pulse rate of 78 per minute, respiratory rate of 20 per minute, temperature of 98.4 F., and weight of 80 Kg. with no history of recent weight loss. There was a firm bilobular mass in the right lower abdomen extending to a level slightly above the umbilicus and slightly tender to manipulation, particularly on bimanual pelvic examination. The external genitalia, vagina and cervix were not unusual. The remainder of the physical examination was essentially negative.

The laboratory data were as follows: Urinalysis was essentially negative. Examination of the blood revealed 10.7 Gm. of hemoglobin, red blood count of 3,130,000, and white blood count of 4,050 with 44 per cent polymorphonuclear neutrophilic leukocytes, 54 per cent lymphocytes and 2 per cent monocytes. A flat plate of the abdomen revealed a lower abdominal mass with a roughly oval-shaped calcified area measuring 5 by 3.5 cm.

The clinical impressions were fibromyomata uteri and/or right ovarian cyst.

An exploratory laparotomy was performed on the third hospital day under general anesthesia through a suprapubic paramedian incision. A right tubo-ovarian mass was encountered, the tube being elongated and retort-shaped. The tubo-ovarian mass, left tube and body of the uterus were excised. The ovarian cyst was ruptured during the operative procedure.

Pathological examination revealed a papillary adenocarcinoma of the right fallopian tube, which measured 25 cm. in length and up to 5 cm. in diameter, extending into the right cornu of the uterus. The neoplasm projected from the fimbriated end of the tube which opened into a previously opened ovarian cyst without proper lining, measuring some 10 cm. in diameter. The neoplasm was friable and there were numerous foci of necrosis. There was slight pleomorphism of the neoplastic cells and an occasional tumor giant cell was present. The nuclei were large and slightly vesicular. Scattered mitotic figures were present. The cytoplasm was scanty in amount. The anaplastic cells were arranged in sheets with papillary formation for the most part; however, there were foci of gland formation and solid masses of anaplastic cells. Clumps of neoplastic cells were present in the lumens of several of the veins in the wall of the tube. The wall of the tube, however, was not perforated by the neoplasm.

Serosal adhesions bound the tube to the ovarian cyst wall which averaged 0.6 cm. in thickness. There was a moderate amount of old blood clot and fibrin attached to the inner wall of the cyst.

There was residual salpingitis of the left tube which was distended to a diameter of 2 cm. and was filled with bloody fluid (hematosalpinx). There was fibrosis of the wall; the fimbriated end of the tube was sealed. Scattered leukocytic infiltration and a few pigment-laden macrophages were present in the wall of the tube.

Serosal fibrous adhesions of the body of the uterus which was enlarged to 10 by 8 by 8 cm. by multiple interstitial and subserous fibromyomata, the largest fibromyoma was a pedunculated subserous one measuring 4 by 2.5 cm. The endometrium was acyclic in type. A focal area of metastatic papillary carcinoma 1 cm. in diameter was present in the endometrium. Invasion of the myometrium was superficial.

The postoperative course was uneventful. The patient was discharged on the twenty-first hospital day. A follow-up study on this patient was not available.

Discussion

A review of the literature reveals the incidence of primary carcinoma of the fallopian tube to constitute between 0.1 and 0.5 per cent of the female genital cancers as quoted by various authors. Lofgren,[7] with the largest single series of 16 cases, reported an incidence of 0.16 per cent while Hu and others,[2] with 12 cases, reported an incidence of 0.31 per cent of all malignant neoplasms of the female genital tract.

Our 2 cases, aged 42 and 53 years, fell within the age range of most of the reported cases which generally range between 40 and 60 years.

There was no history of pregnancy in the two cases herein reported.

The menstrual history in both of our cases was within usual limits during the childbearing period. Case 1 was 12 years postmenopausal and case 2 had had menstrual irregularity characterized by periods of amenorrhea for one year prior to hospitalization. Both cases complained of vaginal discharge at various times.

Large tumor masses had developed in both of these cases with the production of very few symptoms. Due to the silent nature of this kind of neoplasm, the patient does not seek medical advice until the malignancy is far advanced. We feel that this explains the high recurrence rate following surgical intervention.

In one of our cases, the vaginal and cervical films stained by the Papanicolaou method revealed no malignant cells. This cytological study has been suggested as an aid in the diagnosis of carcinoma of the fallopian tube. A negative report, however, has little significance.

The diagnosis of primary carcinoma of the fallopian tube is rarely made preoperatively. Most of the reported cases have been diagnosed as fibromyomata, tubo-ovarian masses and ovarian cysts. There are no characteristic and very few suggestive findings which might indicate a correct diagnosis. Both these cases herein reported

were diagnosed as fibromyomata uteri; an ovarian cyst was also suspected in case 2.

The gross pathology in many of the cases reviewed appears to be similar. The neoplasm may enlarge the tube slightly or form large masses which usually conform to the shape of the tube. Most of the carcinomas have not perforated the wall of the tube but distend the lumen, project from the fimbriated end or, in a smaller percentage of cases, extend into the endometrial cavity either by direct extension or implantation. The neoplasm may extend to the vagina by direct extension, lymphatic permeation or by implantation in some cases. Residual salpingitis or salpingitis has been associated in a large percentage of cases and a tubo-ovarian mass may have developed in the course of the infectious process. The distal one-half of the tube is usually involved by the malignancy.

Microscopic findings vary with the degree of malignancy from an early papillary type in which the papillary processes are covered by anaplastic columnar type cells, to an intermediary papillary adenocarcinoma with the formation of numerous atypical glands some of which form papillary processes, or to an advanced adenocarcinoma formed mainly by solid masses of cells which may attempt to form papillary processes and glands. Different areas in case 1 exhibit all three of these types and case 2 is formed by a combination of the latter two types.

The accepted therapy is surgical extirpation in the operable cases. A combination of surgery and postoperative irradiation therapy has been used in the majority of cases. More advanced cases and recurrences may be treated with palliative irradiation therapy.

We wish to express our appreciation to Mr. Orville A. Parkes, Professor of Department of Medical Illustration of the Medical College of Georgia, for the illustration of the surgical specimen in case 1.

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PULMONARY EMBOLUS: POSTOPERATIVE INVESTIGATION OF TRENDELENBURG POSITION FOR PROPHYLAXIS

RICHARD TORPIN, M.D.*
Augusta

WITHIN a short time, in the year 1940, we had 2 cases of fatal pulmonary embolus, both proved by autopsy. One followed vaginal hysterectomy in a white woman and occurred on the twelfth postoperative day. She had early ambulation of a rather violent type since she became psychotic soon after the operation and was up much of the time. The other, a negro woman, followed abdominal hysterectomy and occurred ten days or so after operation. At that time it occurred to me that massive embolus might be impossible if there was no stagnant blood in any venous bed, and it was decided that postural drainage of the pelvic region as well as of the deep veins of the leg might be beneficial in preventing development of a clot which may become detached as an embolus.

From that time until the present all patients on our gynecologic service, both staff and private, were treated postoperatively by elevation of the foot of the bed at least 8 inches for 96 hours.

During that subsequent period of 10½ years there have been approximately a total of 150 major gynecological operations per year; most of these involved hysterectomy. There have been no instances of proved pulmonary emboli and no deaths suggesting such complication. There have been no complications due to the rather awkward position. Seldom does a patient make any complaints or even comment although they seem to be pleased when the foot of the bed is lowered on the fourth day.

We have been in full agreement with the theory of early ambulation and since its recent revival all patients are treated in accord with this principle. They are urged to be up as soon as feasible, the day after the operation if they so desire. However, when in bed they resume the head-low position during the first four days.

We pay considerable attention to Homans' sign, pain, cyanosis or edema. We require consultation on all cases of thrombophlebitis and of suspected phlebothrombosis and have available consultants who are thoroughly versed in the application of anticoagulants or surgical therapy of possible emboli.

Upon reviewing the literature to ascertain other experience with

From the Department of Obstetrics and Gynecology, Medical College of Georgia.
*Professor of Obstetrics and Gynecology.

postural prophylactic management of the postoperative patient, it was found that the first mention of a similar method at least in the American literature was by H. K. Gray[1] who in 1934 reported the results of 276 patients who were placed in the Trendelenburg position (elevation of the foot of the bed 10 inches) for the first 24 hours after abdominal operations unless there was intra-abdominal drainage, suppurating process or when such a position would embarrass respiration as in a weakened myocardium. He drew attention to its theoretical benefits in preventing tracheobronchial aspiration and retention of secretions and reported a reduction of 30 per cent in all pulmonary complications over that of a control group, but states that the series was small. There was no fatal embolus.

In 1940 G. de Takats and J. H. Jesser[2] reported upon a similar study. They stated that "the survey of large collective statistics reveals a fairly steady incidence in large services, namely from 0.1 to 0.2 per cent of all operations, 2 per cent of all deaths, 6 per cent of postoperative autopsies." They studied 100 bona fide records and found 25 were medical, 74 surgical and one obstetric. Among the surgical group pelvic laparotomy led with 33 of the 74.

Noting Gray's paper, they state, "In the last five years (1934 to 1939) 350 patients have been placed in this position at St. Luke's Hospital (Chicago) and the Illinois Research and Educational Hospitals. There was no postoperative thrombosis in this group and the incidence of pulmonary complications as detected by clinical examination was 3 per cent. At the same time a group of 1,000 surgical cases at these institutions showed 5 cases of postoperative thrombosis. It was difficult to get adequate data of postoperative pulmonary complications, but they were marked in the charts in 28 per cent. It is obvious that our limited material is not well comparable to the control groups, as there were no pelvic laparotomies or prostatic operations on aged patients among the 350 cases; while suggestive, it does not permit any conclusions."

In 1941 Potts and Smith[3] attempted to determine whether the reasoning back of the clinical application of postoperative exercises could be substantiated by a series of experiments on 6 dogs. They reported in part, "Simultaneous elevation of both hind legs of the dog produced an increase varying from 100 to 150 per cent in the volume flow of the blood in the inferior vena cava. In animals rather lightly anesthetized, contraction of the muscles in both hind legs occurring coincident with their elevation produced an increase of more than 250 per cent in the volume flow. The increase in the volume flow was abrupt and returned to normal in 10 to 15 seconds. To check the accuracy of our observations, the femoral veins were isolated just below the inguinal ligament and clamped. Elevation

of the legs then produced practically no change in the volume of blood flow. Removal of the clamps was followed by a prompt increase in flow."

de Takats and Fowler[4] in 1945 stated, "Elevation of the foot of the bed on chairs or on shock blocks is an excellent, simple procedure to accelerate venous return from the lower extremities. The pelvis must be included in this reversed drainage."

Homans[5] stated in 1947, "Elevation of the foot of the bed favors a return circulation and avoids venous stasis. Combined with exercise in bed, this procedure has a favorable influence on thrombosis already established. It should therefore be useful as a preventive measure."

Comment and Conclusions

Evidence has been presented in favor of the Trendelenburg position applied immediately postoperatively in pelvic surgery for its prophylactic effects in preventing phlebothrombosis and fatal pulmonary embolus. While the evidence is meager and mainly negative, there was no fatal pulmonary embolus in approximately 1,575 hysterectomies. The method is extremely simple, requires no additional nursing attention, apparently causes no harm except possible temporary inconvenience to the patient, and as Gray stated, tends to reduce all pulmonary complications. It ought to receive wider attention in attempts to abolish the specter that attends every surgeon in even the most minor operation.

By now the value of the method might have been assayed had it not been that the more spectacular anticoagulants and veinsection operations occupied the attention of the profession in the past decade.

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EXPERIMENTAL STUDIES ON TORULOSIS

Part I: Preliminary Experiments on Therapy

LOUIS O. J. MANGANIELLO, M.D.*
Augusta

ALTHOUGH the clinical syndrome and pathologic aspects of torulosis have been fairly well established, little investigation of this condition has been done in the experimental therapeutic field. This paper contains certain observations which are neither complete nor well established. Nevertheless, they will act as a starting point from which more accurate and controlled experiments may be commenced. These facts are presented solely for the purpose of recording a wide range of preliminary observations with the intention of stimulating an interest in a rather virgin field.

The organism used in this study was obtained from the spinal fluid of a patient in the University of Maryland Hospital. It was identified by the Bacteriological Department as Cryptococcus Hominis. A diagnosis of torula meningitis was made and was confirmed by autopsy six months later. The experimental animals used were C3H mice and rabbits.

Freeman[2] has called attention to the low toxicity and the almost complete lack of inflammatory response seen in torulosis. He has attributed its chronic but fatal clinical course to these facts. If some agents could be used to stimulate the production of inflammatory cells in the presence of a torula infection, this would convert the disease from a chronic to an acute one. It was hoped that the cellular response would enable the host to cope with and destroy the pathogenic yeast. Aleuronat in a 2 per cent sterile solution was first used. This was administered intraperitoneally 48 hours after the mice had been injected by the same route with a torula suspension. This had been prepared by centrifuging a 48 hour broth culture and suspending the sediment in one-half the original volume of normal saline. Smears and cultures were obtained from the peritoneal cavity before aleuronat was given. The experiment was set up according to table I. The leukocytic response was not as dramatic as expected. One mouse was autopsied from each group 48 hours after the initial dose of torula. Cultures were taken in order to establish the presence of the infection. In groups Ia and Ib they were negative. Those in groups II and III were positive. Peritoneal smears made seven days later showed some leukocytosis in group I. In group II there was some suggestion that the organism was sur-

*Dept. of Neurosurgery.
From the Department of Neurologic Surgery, Medical College of Georgia.

rounded by inflammatory cells. Group III showed no leukocytic stimulation. Although the aleuronat treated mice survived longer than the nontreated group, it was felt that the efficacy of aleuronat was equivocal.

TABLE I

Group	#Mice	Torula Suspension	Aleuronat	Culture	Dead in 7 12 17 25 days
Ia	2	None	1 cc.	0	0 0 0 0 (2 mice autopsied)
Ib	4	None	0.5 cc.	0	0 0 0 0
II	4	0.5 cc.	0.5 cc.	X	0 1 2 all (2 mice autopsied)
III	5	0.5 cc.	None	X	5 (2 mice autopsied)

In the next experiment 25 mice were used. The same torula suspension and the following agents were used: (1) 5 per cent solution $NaHCO_3$; (2) Para-aminobenzoic acid, 10 mg./cc.; (3) Anesthesin* 10 mg./cc. in 6 per cent Acacia solution, and (4) combination of (1) and (2). (See table II.)

It was noted by Mosberg[3] that pH was a factor controlling the growth of torula, the more alkaline the media, the more inhibited in growth was the organism. In this experiment the mice received PAB with a pH of 3.8-4, all died by the seventh day; those receiving PAB and $NaHCO_3$ by the tenth day, whereas, those given $NaHCO_3$ (pH 8.4) alone, all died by the twenty-fifth day. On the other hand, the mice receiving anesthesin all survived. Peritoneal cultures were taken 48 hours after initial injection and before treatment was started. These were positive; but final cultures at the end of the experiment were positive in only four of the five groups. The anesthesin group was free of torula. The leukocytic response was most pronounced with anesthesin. It was concluded that anesthesin had definite antitorula properties, but was nevertheless toxic. Again pH seemed to be an inhibitory factor in torulosis.

The next method of attack was an attempt to use immune rabbit serum as a therapeutic measure. However, it was first thought advisable to test the agglutinating properties of such a serum. This serum was prepared in the following manner. Six rabbits were used. Three of these were given intravenously 0.25 cc. of the routine torula suspension which had been treated according to the Benham's[1]

*Ethyl amino benzo-Benzocaine.

TABLE II

Group	Number of Mice	Torula Suspension	Agent; pH q. 2d. for 4 doses	48 hr. Culture	Leuko, Res.	Number dead in number of days 7 10 25	Final Autopsy Culture
I	5	0.5 cc.	0.5 cc. $NaHCO_3$ pH 8.8	X	XXX	0 3 all	X
II	5	0.5 cc.	0.5 cc. PAB pH 3.8-4.0	X	?	all	X
III	5	0.5 cc.	0.5 cc. PAB & $NaHCO_3$; pH 8.5	X	XX	0 all	X
IV	5	0.5 cc.	Anesthesin 0.5 cc.; pH 8.2	X	XXXX	0* 0 0	0
V	5	0.5 cc.	0	X	0	all	X

*Three of the anesthesin mice died immediately after injection aesin was reduced to 0.25 cc.
cavity. Three other mice were substituted but the dose of anesthnd autopsy showed simply an excess of fluid in the peritoneal

method with HCl. These rabbits were given also 2.5 cc. of the same torula suspension intraperitoneally. The remaining 3 rabbits were given the same doses of the routine torula suspension with HCl treatment. All 6 rabbits were injected every other day for a total of three doses, the intraperitoneal dose remaining constant, the intravenous dose being doubled each time. Seventeen days after the initial injection all rabbits were bled. Agglutination tests were set up in the following manner and read after 48 hours (table III). The results indicate there was some immunologic response in the rabbits although the agglutination of the sera was not too great. The most pronounced was noted in group A which substantiates Benham's[1] work along these lines in mice.

TABLE III

Group A) *Serum from Treated Organism and Treated (HCl) Organism*					
Dilution	1/20	1/40	1/80	1/160	1/320
Agglutination	X	XX	XX	XX	XXXX
Group B) *Serum from Treated Organism and Untreated Organism*					
Dilution	1/20	1/40	1/80	1/160	1/320
Agglutination	X	XX	XX	XXX	XXX
Group C) *Serum from Untreated Organism and Treated Organism*					
Dilution	1/20	1/40	1/80	1/160	1/320
Agglutination	X	XX	XX	XX	X
Group D) *Serum from Untreated Organism and Treated Organism*					
Dilution	1/20	1/40	1/80	1/160	1/320
Agglutination	XX	XX	XX	X	XX

The sera were now subjected to a therapeutic trial. Sixty mice were injected intraperitoneally with 0.5 cc. of the routine torula suspension. Three days after initial injection 3 mice were picked at random and autopsied. Peritoneal smears and cultures were made which proved positive for torula. A week after initial injection, therapy was started in the following manner. Twenty were given no treatment at all, 20 were given 0.5 cc. dose of immune rabbit serum intraperitoneally every day, and 20, 0.25 cc. of immune rabbit serum and 0.25 cc. of fresh guinea pig serum daily intraperitoneally. Therapy was continued for a week. Sixteen days after initial injection all mice were dead except those treated with combined rabbit serum and fresh guinea pig serum. All mice in this last group were dead in a month after their initial injection. It seemed that whereas immune rabbit serum had little protective value when used alone, the immune rabbit serum-guinea pig serum

combination seemed to prolong the life of the infected mice. Microscopic secretions of the abdominal organs revealed numerous organisms in the kidneys, spleen and liver. The brain revealed a typical meningoencephalitis with cyst formation.

Another experiment was set up using 110 mice which were injected intracerebrally with 0.1 cc. of torula suspension. Treatment was begun four days after injection using PAB, anesthesin, and immune rabbit serum. Anesthesin in a 1 per cent solution and PAB in a 5 per cent solution was administered orally in the drinking water. Immune rabbit serum was given, 0.5 cc. daily doses. Treatment was continued until all animals died. Within 15 days all animals were dead. Cultures, smears and sections revealed the typical torula organisms and lesion. The drugs used in this manner seemed to be of little aid in combating this disease. It was encouraging, however, to note that there was a 100 per cent infection rate in the animals injected by this intracerebral technique.

SUMMARY

1. A brief résumé of various experiments with torulosis has been presented.

2. PH seems to be a factor in the growth of torula.

3. Mice can be easily and primarily infected with intracerebrally administered torula.

4. Immune rabbit serum seems to be more effective if guinea pig serum is used with it.

5. Anesthesin injected intraperitoneally seems to be effective in torula infection.

6. Orally administered PAB and anesthesin seem to be of little therapeutic value.

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LYMPHOGRANULOMA VENEREUM (INGUINALE), A PRECIPITATING CAUSE OF CARCINOMA

Statistical Analysis of one hundred and thirty-five cases of carcinoma of penis, vulva and anorectum

EDGAR R. PUND, M.D.*
GEORGE R. LACY, JR., M.D.**
Augusta

"In our headlong and rewarding pursuit of causation, I should like to see some measure of refinement and sophistication. I would like to see causes differentiated as precipitating, predisposing or perpetuating—some such qualifying adjective is so often needed. I should like it to be a cardinal axiom of medicine that an organism is so intimate a relationship of constituent parts that you cannot modify any one of them without affecting all the others; and that, therefore, a given result comes usually from not one cause but from a combination of causes, sometimes a sequence, sometimes a constellation or pattern; and similarly that a given cause has not merely one but many results, sometimes in a sequence, sometimes in a pattern."[1]

THIS observation and recommendation of Alan Gregg appertains especially to the study of the causation of cancer. While we are awaiting the discovery of an established cause of cancer, the study of the natural history of this disease must continue in order to recognize cancer in its early stages and to treat precancerous lesions before cancer develops.

The predisposing causes of cancer, with the exception of time, are largely inherent, such as, heredity, race, sex and constitution, individual factors associated with disturbed metabolism and distorted responses to various hormones, either in a state of balance or imbalance. The precipitating causes are numerous and many are well known: physical agents such as actinic rays, x-rays and thermal rays; chemical agents, such as exposure to coal tar products and various types of oils; chronic irritation and trauma, bacterial infection, protozoal infestation and virus infection. Of the perpetuating causes we know little but it is in this last group that lies hope for the discovery of definite prevention and cure of malignancy. In the meanwhile an understanding of the precipitating causes is essential for early recognition and prevention of cancer.

In our study of the pathology of the various venereal diseases, our attention was directed early to the frequency of superimposed cancer.[2] We have previously emphasized the necessity of ruling out carcinoma in suspected venereal lesions of the genitals.[3] Furthermore, we have especially noted an undue frequency of carcinoma

From the Department of Pathology, Medical College of Georgia.
*Professor of Pathology.
**Assistant Professor of Pathology.

superimposed upon lesions of lymphogranuloma venerum. This disease is caused by a virus, and when untreated, runs a protracted course, two features which are considered precipitating causes of cancer. In the male the initial lesion of lymphogranuloma venereum occurs commonly on the penis. When the site of the primary lesion is accessible to cleanliness, the initial sore frequently proves evanescent; however a regional lymphadenitis may result which usually subsides without residua. On the other hand, if the primary sore occurs in the urethra or on the mucosal surface of a redundant prepuce, it is not uncommon to find a lesion which persists over a period of years and which, sooner or later, is associated with lymph stasis and elephantiasis. In the female the primary lesion most commonly occurs on the mucous surface of the vulva or within the vagina. The initial lesion may persist and progress to a subacute or chronic stage with resulting elephantiasis of the vulva, stricture of the vagina or urethra, or, there may be extension to the anus with subsequent stricture.[4]

A study of the lesions of lymphogranuloma venereum in the chronic state will frequently demonstrate a sequence of epithelial patterns from hyperplasia to dyskaryosis to neoplasia. The epithelium of the involved area constantly shows hyperplasia with a considerable degree of acanthosis. Dissociated intra-epithelial anaplasia or dyskaryosis is characterized by a scattering in the hyperplastic epithelium of cells with large and sometimes double nuclei, and a large number of halo cells, a type which is frequently seen in virus infections. Dyskaryotic changes may be multicentric and it is not uncommon to find that cancers develop at these sites which, in their initial stage, may be preinvasive and also multicentric in origin. In the absence of invasion, preinvasive carcinomas are recognizable because the morphology of the cells in all respects is similar to that found in invasive cancer. Imperfect differentiation or even complete loss of polarity, increase in the nuclear-cytoplasmic ratio, bizarre mitotic figures, anisokaryosis, the presence of prominent nucleoli, nuclear vesicularity and hyperchromatism, and basophilism of the cytoplasm are the main criteria for recognition. Before invasion takes place, the carcinoma can be eradicated because there is little likelihood for metastases to occur so long as the carcinoma is confined to natural surfaces. The possibility of penetration of the lymphatics or blood vessels is remote.

For the past several years we have been interested in lymphogranuloma venerum as a precipitating cause of cancer and we have endeavored to obtain the cooperation of clinicians in securing Frei tests on patients who have lesions of the genitals and of the anus. We have been fortunate indeed in having the cooperation of the

staff of the Alto Venereal Disease Center of the State of Georgia for whom it has been our privilege to act as consultants in pathology. We have reviewed our cases of carcinoma of the penis, of the vulva and of the anorectum since July 1937, a period of approximately 15 years. A total of 135 cases have been reviewed (table 1). Unfortunately a Frei test was not performed on any of the 50 white patients.

Table 1

CARCINOMAS REVIEWED

POSITIVE FREI TEST USED AS CRITERION FOR DIAGNOSIS OF LYMPHOGRANULOMA VENEREUM

		Positive Frei	Negative Frei	Frei Not Done	Total	Positive Chancroid	Pos. Chancroid Pos. Frei	% Frei Positive L G V	
Penile Carcinoma	White	0	0	28*	28-40%	1	0	0	26%
	Negro	18*	7	17**	42-60%	6	4	43%	
Vulvar Carcinoma	White	0	0	20*	20-37%	0	0	0	15%
	Negro	8	11*	15	34-63%	7	5	24%	
Ano-Rectal Carcinoma All Females	White	0	0	2	2-18%	0	0	0	45%
	Negro	5	0	4	9-82%	1	1	56%	
Totals	White	0	0	50	50-37%	1	0	0	23%
	Negro	31	18	36	85-63%	14	10	36%	

*Each asterisk denotes a preinvasive carcinoma in the indicated group

Of the 70 patients with carcinoma of the penis, 18 reacted positively to Frei antigen (26 per cent). In this group there were 42 negroes and in 18 (43 per cent)the Frei test was positive. Eight (15 per cent) of the 54 patients with vulvar carcinoma and 5 (45 per cent) of the 11 with anorectal carcinomas reacted positively. If the white patients are not included because of failure to secure a Frei test, we observed that 24 per cent of negro patients with vulval carcinoma and 56 per cent of negro patients with anal carcinoma reacted positively. It is interesting to note that all carcinomas of the anorectum in this series occurred in females. When the entire group is considered, 23 per cent of 135 patients with penile, vulvar or anorectal carcinoma had positive Frei tests and 36 per cent of the 85 negro patients.

The surgical material sometimes included sufficient material for pathologic study which permitted histologic appraisal as to the probable existence of an underlying lesion of lymphogranuloma venereum (table 2). In 4 (14 per cent) white patients with penile carcinoma the inflammatory reaction was strongly suggestive of lymphogranuloma venereum. In none of the patients was a Frei

test performed. In 1 negro case of penile carcinoma with a negative Frei test and in 7 cases without Frei tests the histology could be considered positive. If these 8 cases are added to the 18 cases with positive Frei, then the 26 patients who exhibit manifestations of lymphogranuloma venereum represent 62 per cent of all negro patients with penile carcinoma. The total percentage for cases of penile carcinoma with some criterion for diagnosis of lymphogranu-

Table 2

POSITIVE FREI TEST AND HISTOLOGY USED AS CRITERION FOR DIAGNOSIS OF LYMPHOGRANULOMA VENEREUM

		No of Cases	Pos Frei	Pos. Histology No Frei	Pos. Histology Neg Frei	% with Probable L G V	
Penile Carcinoma	White	28	0	4	0	14%	43%
	Negro	42	18	7	1	62%	
Vulvar Carcinoma	White	20	0	0	0	0	30%
	Negro	34	8	5	3	47%	
Ano-Rectal Carcinoma	White	2	0	0	0	0	45%
	Negro	9	5	0	0	56%	
Totals	White	50	0	4	0	8%	38%
	Negro	85	31	12	4	55%	

loma venereum is 43 per cent. In 5 negro cases of vulvar carcinoma without Frei tests and in 3 with negative Frei tests, the inflammatory reaction was suggestive, which when considered together with the cases with positive Frei tests represent 47 per cent of negro patients and 30 per cent of all patients with carcinoma of the vulva. No additional information was obtained from the histologic reaction in patients with anorectal carcinoma. When histology and a positive Frei test are used as criteria for diagnosis, we find that in 38 per cent of all cases of carcinoma included in this study there was evidence of coexisting lymphogranuloma venereum. This includes 8 per cent of white patients and 55 per cent of the negro patients.

The relationship that lesions of lymphogranuloma venereum bear to carcinoma can be further emphasized if only those cases are considered who have been subjected to a Frei test (table 3). Eighteen (72 per cent) of 25 cases of penile carcinoma, 8 (42 per cent) of 19 vulvar carcinomas and 5 (100 per cent) of anorectal carcinomas had positive tests. A total of 49 cases with carcinoma

of penis, vulva or anorectum were tested with Frei antigen and 31 (63 per cent) reacted positively.

Table 3

CASES OF CARCINOMA IN PATIENTS WITH FREI TESTS
ALL NEGROES

	No of Cases	Pos. Frei	Neg. Frei	% Pos Frei L.G.V.
Penile Carcinoma	25	18	7	72%
Vulvar Carcinoma	19	8	11	42%
Ano-Rectal Carcinoma All Females	5	5	0	100%
Totals	49	31	18	63%

We feel convinced that the coexistence of lymphogranuloma venereum in a large percentage of patients with carcinoma of the penis, vulva or anorectum is not fortuitous. We do not believe that this relationship is paralleled by any other venereal disease. While it is accepted that carcinoma of the tongue occurs at a higher rate in syphilitics than in nonsyphilitics, we do not believe that the rate would in any way approach the proportion of genital and anorectal carcinomas which are found in patients with lymphogranuloma venereum. Pre-existing syphilis is rarely incriminated as a precursor of genital cancer. Gonorrhea can be considered a negligible factor in the causation of cancer. The urethra, vulvovaginal glands and Fallopian tubes, while the common sites of gonococcus infection, are relatively rare sites for carcinoma. We have had the opportunity of observing a large number of patients with granuloma venereum. We have on file only 2 patients with this disease with coexisting carcinoma, one of the cervix uteri and one of the penis. It is true, however, that errors of diagnosis may occur because "pseudo-epitheliomatous" proliferation of the epithelium is commonly observed in granuloma venereum. It is possible that the chronicity of chancroid inflammation may predispose to genital cancer. To determine if this played any part in the development of carcinoma in this series, we have tabulated the number of patients with positive Ducrey antigen tests in this series (table 1). While

we do not deny the possibility of cause and effect in chancroid, it is interesting to note that of the 14 patients in this series with positive Ducrey tests, 10 also had coexisting positive Frei tests and in one patient with a positive Ducrey test no Frei test was performed. Our offhand experience does, however, indict the venereal wart as a precancerous lesion, but our surgical material is limited because of nonsurgical methods of treatment. We are also cognizant of the part played by a redundant prepuce in carcinogenesis. This of course may account for the excessive number of penile carcinomas in the series, but it has no relation to the carcinomas of the vulva or anorectum. It does, however, contribute to the chronicity of lesions of lymphogranuloma in the male.

In this study we have offered evidence which supports our concept that persistent lesions of lymphogranuloma venereum should be considered as precancerous lesions and that lymphogranuloma venereum is one of many predisposing causes of carcinoma.

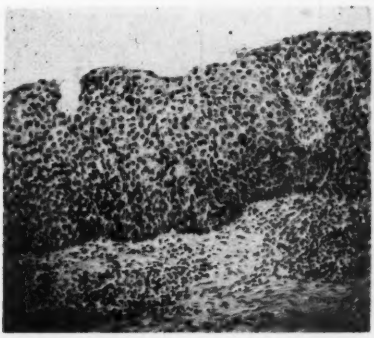

Fig. 1. Carcinoma of anal canal at site of stricture. Note that the carcinoma is confined to the natural surfaces in this area (preinvasive).

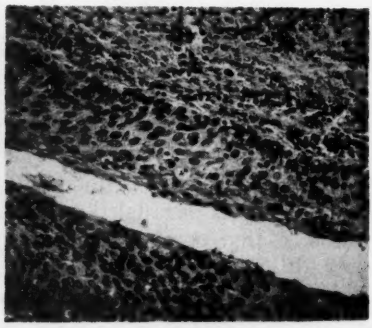

Fig. 2. Sinus tract lined with cancerous epithelium similar to that in figure 1.

Illustrative Case

A negro female, aged 33, complained of pain and difficulty in defecation. A change in bowel habits had been noticed for about 15 months. Bouts of constipation had been followed by diarrhea and recently pain on defecation had developed. There had been a progressive decrease in the diameter of the stool and at present they were of lead-pencil size. Between the bouts of constipation and diarrhea, she experienced two or three small movements per day and occasionally blood was noted in the stool. Her past illnesses included gonorrhea nine years previously and "bad blood" five years ago, both of which had been treated. She was married but had never given birth to children. She appeared anemic and undernourished and the hemoglobin was 8.5 Gm. Two small fibrous anal tabs (lymphorrhoids) were noted and 2 inches above the sphincter the lumen of the rectum was fixed and contracted by a firm stricture. The

proctoscope could be introduced only a distance of 5 cm. and the stricture appeared gristly and grayish in color. Because of the density of the tissue, a biopsy was secured with difficulty. Examination of the biopsy revealed a squamous cell carcinoma in the small section which was obtained. The Frei test was positive. The Kahn test was also positive at a dilution of 1:16. Supportive therapy and blood transfusions were administered in preparation for an abdominoperineal resection. Two weeks after admission a combined abdominoperineal resection was performed.

The patient had a rather stormy postoperative course and required repeated transfusions. She was dismissed, however, two weeks after the operation. Five months later it was necessary to increase the size of the colostomy because of fibrous constriction; however, examination of the colostomy opening revealed no evidence of the carcinoma nor was there any evidence of the extension of the inflammatory process as was seen in the rectum.

Fig. 3. Area of invasive carcinoma of anal canal. Note that the tract is in part ulcerated and granulating.

Pathologic Examination: The section of rectosigmoid including a cuff of perianal skin 3.5 cm. wide was 17 cm. in length. Proximal to the squamocolumnar junction of the anus there was a stricture 8 cm. long with extreme narrowing of the lumen. The surrounding soft tissues in the region of the stricture were considerably indurated and a number of sinuses extended into the soft tissues. At the site of the stricture the anorectum was in part ulcerated and granulating and in part covered with anaplastic stratified squamous epithelium which also partly lined many of the sinuses (figs. 1 and 2). The epithelium was composed of imperfectly differentiated squamous cells with all the characteristics of the cells of squamous cell carcinoma. In most areas the carcinoma was confined to the natural surfaces of the lumen of the bowel or of the sinuses; however, in several areas there was superficial invasion of the underlying soft tissues (fig. 3). Invasion was never extensive. Chronic inflammatory changes, characterized by pronounced fibrosis and dense perivascular inflammatory cell infiltrate, chiefly of plasmacytes, were observed in the wall of the anus and rectum. The pathologic diagnosis was: "Squamous cell carcinoma of anorectum superimposed upon a rectal stricture of lymphogranuloma venereum."

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MALIGNANT MELANOMA OF THE GASTROINTESTINAL TRACT

A Case Report

A. B. CHANDLER, M.D.*
G. FRANK JONES, M.D.**
Augusta

WE WOULD like to present the following case of malignant melanoma of the gastrointestinal tract.

History: A 64 year old white male complained of nausea, eructation and anorexia which had been increasing in severity over a period of three months. He had also suffered from occasional pains over the precordium and in the right upper quadrant of the abdomen. There was a weight loss of 15 pounds, from 150 to 135 pounds.

Physical examination at this time revealed marked tenderness in the right upper quadrant of the abdomen. This pain was intensified by respiration.

Roentgenological studies were then carried out in order to further evaluate the case. These presented the following: (1) suggestive small gastric ulcer 1 mm. in depth and 2 mm. in breadth on lesser curvature midway between cardia and angle, (2) renal calculi, bilateral, (3) hypertrophic arthritis of the lumbar spine, and (4) no gallbladder pathology.

The patient was referred to an internist and a strict medical regime was instituted. Not responding to treatment, he returned four months later appearing chronically ill and in rather poor condition. He complained of epigastric discomfort, weakness and progressive loss of weight. The patient showed signs of considerable weight loss. No abdominal masses, distention or rigidity were evident. A repeat x-ray examination was done, and at this time multiple polypoid masses in the upper two-thirds of the stomach were demonstrated, suggestive of a rapidly growing fungating carcinoma or a leiomyosarcoma. The patient was given a protein dietary supplement as well as multiple blood transfusions in order to prepare him for surgery. Shortly thereafter, his condition was thought satisfactory for surgical exploration.

The preoperative laboratory data in the hospital were as follows: Hb. 12.4; R.B.C. 3,650,000; white blood count 6,700, with neutrophils 45 per cent, lymphocytes 45 per cent, monocytes and eosinophils 1 per cent. Urine was not remarkable. Chemistry: NPN 25; Nacl 439; total protein 5.7; albumin fraction 3; globulin fraction 2.7.

Operation was performed through a long, high, left transrectus incision. In addition to the gastric lesion, small dark masses were in the gastrocolic ligament and the mesentery of the transverse colon, measuring up to 0.5 cm. in diameter. Four palpable hepatic nodules were estimated to be 1 to 2 cm. in diameter. Some 12 nodules were palpable in the jejunum and ileum; the largest being in the terminal ileum. This mass was resected and an end-to-end

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From the Departments of Pathology and Surgery, Medical College of Georgia.
*Resident, Pathology.
**Associate Professor of Surgery.

anastomosis performed. A gastric resection was then carried out, removing approximately seven-eighths of the stomach, and an open gastrojejunostomy was established. The greater omentum was removed with the stomach. The wound was closed anatomically without drainage.

The patient had a fairly uneventful recovery, having developed a wound infection which healed well. He was discharged from the hospital on the twenty-sixth postoperative day. Thereafter, he pursued a downhill course and died in his home one month later. Permission for autopsy was not obtained.

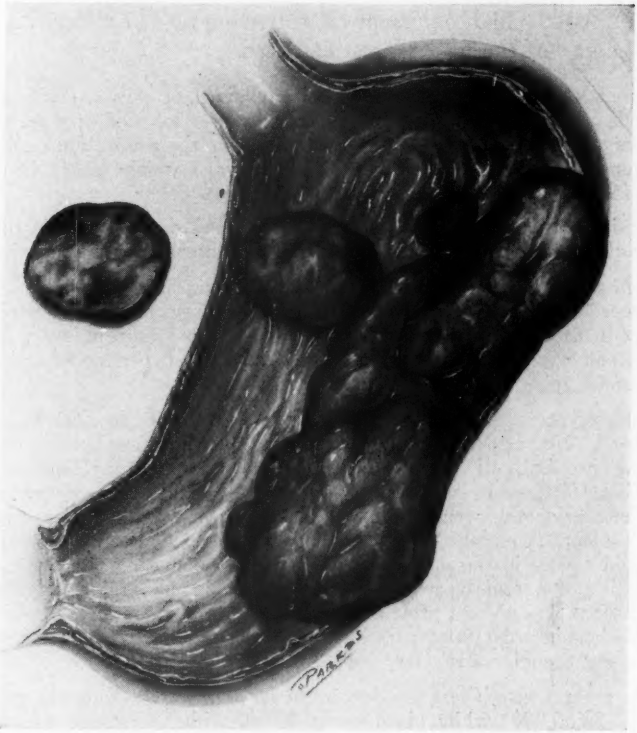

Fig. 1. Artist's reconstruction of formalized and previously opened specimen with a cross section of one of the polyps on the left.

The pathological report was as follows: Malignant melanomas of the stomach forming six polypoid masses mainly involving the mucosa of the stomach but showing invasion at the base. One fungating polyp is 9 by 5.5 by 2.5 cm. and arises on the lesser curvature 2 cm. from the proximal line of excision. Another large polypoid neoplasm 10 by 6 by 2.5 cm. arises on the greater curvature 2.5 cm. from the proximal surgical margin. On the posterior wall there is an additional one 4.5 by 7.5 cm. and 3 cm. high, 2.5 cm. from the proximal margin. These three polyps are in close approximation and the adjoining edges are faceted. Smaller polyp 1.5 cm. in diameter is on the posterior surface near the midpoint of the stomach. Similar tumor 4.5 cm. in

diameter and 1.5 cm. high on the greater curvature arises 6 cm. from the distal margin. Deeply pigmented polypoid neoplasm 2 cm. in diameter is on the greater curvature 3 cm. from proximal surgical margin, and an additional deeply pigmented polypoid neoplasm 1 cm. in diameter is 4 cm. from the proximal surgical margin. Ulcerated malignant melanoma 3 by 4 cm. with raised edges is present in the section of ileum 7 cm. long; secondary nodule 0.3 cm. in diameter is on the serosa. Three metastatic nodules 0.5 to 1.2 cm. in diameter are in the omentum and three metastatic nodules each 0.8 cm. in diameter occur on the lesser curvature of the stomach.

Discussion

This case is interesting in that it demonstrates a comparatively rare lesion of the gastrointestinal tract; the rapidity of development with widespread visceral metastases is rather striking. Katz in December of 1950 reported the thirty-second case in the literature. Of these, 22 were definitely metastatic lesions and the exact nature of some of the remaining was in doubt. Willis in his text states that he has never seen reported a case of melanoma of the viscera which definitely had ruled out all possible sources of a primary lesion elsewhere. Although no other primary source was demonstrated in this case, a metastatic lesion must be considered. An autopsy would have been of interest.

It is conceivable, however, that this neoplasm may have originated in the gastric submucosa. A terminal plexus of the sympathetic nervous system, Meissner's plexus, is situated in the submucosa.[2] Chromaffin tumors, especially of the suprarenals, may resemble an amelanotic melanoma. Pigmented tumors which cannot be differentiated from melanomas elsewhere have also been observed in the suprarenal.[3] Melanoblasts, which are derived from the neural crest,[1] are very closely allied to other cells of the neuro-ectoderm such as those of the chromaffin and sympathetic system. It is, therefore, not inconceivable that the neural cells of Meissner's plexus, which have a common origin with those of the chromaffin system and the melanoblasts, could elaborate melanin.

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CLINICAL IMPRESSIONS OF TWO NEW INTRAVENOUS BARBITURIC ACID DERIVATIVES FOR ANESTHESIA

A. J. Waters, M.D.*
Perry P. Volpitto, M.D.**
Augusta

Numerous barbituric acid derivatives have been prepared, yet only five, isoamylethyl barbituric acid (amytal), sodium ethyl (1-methylbutyl) barbiturate (nembutal), sodium isoamylethyl thiobarbiturate (thioethamyl), N-methylcyclohexenylmethyl barbituric acid (evipal), and sodium ethyl (1-methylbutyl) thiobarbiturate (pentothal), have been given extensive clinical trial as intravenous anesthetic agents. All of these have failed to meet the rigid requirements of an ideal anesthetic agent. Each of these seems to sensitize the laryngeal reflexes, so that at times laryngospasm and coughing result. They all cause respiratory as well as circulatory depression. The prolonged postoperative sleep so often seen following administration of relatively large quantities of these agents over long periods of time is common to each of the above barbiturates. Inadequate muscular relaxation may also be mentioned as a minor disadvantage. For these and other reasons the search for new intravenous drugs that might obviate some if not all of these objections seems justified and deserves further investigation.

One of the more recently prepared barbituric acid derivatives, sodium 5 allyl 5 (1 methylbutyl)-2-thiobarbiturate (sodium surital) has been studied in the laboratory with promising results. It differs from the well-known pentothal sodium in the substitution of an allyl group for the ethyl side chain.

Kelly, Shideman and Adams[1] have studied surital on dogs in the laboratory and report that it is 139 per cent as potent as pentothal. The shape and slope of blood level curves of both drugs was found to be similar, indicating approximately equal rates of detoxification. In a more recent study Wyngaarden, Woods, Ridley and Seevers[2] have shown surital to have a potency of 1.5 as compared to 1.0 for pentothal. These workers found that surital produced a more rapid induction of anesthesia than pentothal with fewer signs of excitement and a more rapid recovery. Their studies on laryngeal reflex activity in cats showed no advantage in the use of one drug over the other. There was a definitely lower rate of accumulation of surital

From the Medical College of Georgia.
*Assistant Professor of Anesthesiology.
**Professor of Anesthesiology.

as based on duration of anesthesia following repeated doses of the drug. Woods, Wyngaarden, Rennick and Seevers[3] have studied the cardiotoxic effect of these drugs in heart-lung preparations as well as in intact dogs, employing cardiac output, impairment of cardiac reserve and cardiac failure as indexes. By these studies they have shown that, in equivalent doses, surital is perhaps less, but definitely not more, toxic than pentothal.

Helrich and others[4] published the first clinical report on the use of surital. They state that the agent deserves further practical application in that their observations have supported and extended the experience obtained with experimental animals. They believe the drug to be superior in some respects to similar drugs in current popular use. Among these are the more rapid awakening from a comparable plane of anesthesia, the more rapid restitution of spontaneous breathing after large doses are given rapidly, and an important difference is in the more benign nature of laryngospasm with surital as compared with other barbiturates. Dillon and Denson[5] have reported the use of surital in 700 cases. They state that the outstanding feature of the drug is its similarity of action to pentothal. They did notice, however, that the duration and severity of laryngospasm were not of the intensity ordinarily associated with pentothal and that the awakening time was somewhat less when surital was used. Helrich and others[6] have reported the use of surital in infants and children during endoscopy. They state that the drug is moderately depressant to respiration and produces a lower incidence of severe laryngospasm and bronchospasm than other barbiturates in common usage. Gain and others[7] compare surital with pentothal and find the new drug to be apparently more potent; that there is a more rapid recovery from a comparable plane of anesthesia; that there is less circulatory and respiratory depression, and seemingly a decreased incidence of laryngospasm as well as a more benign nature of laryngospasm when it does occur. Spencer and Coakley[8] in a recent report of 337 cases state that the effects of surital did not appear to vary greatly from those of pentothal. Brinker and others[9] and Kirchhof[10] have recently reported their work with the use of this new agent.

The Anesthesiology Department of the Medical College of Georgia and the University Hospital has had the opportunity to investigate the clinical behavior of this new drug surital sodium.* We here report further clinical experiences in 1,485 cases in which the agent was used either for induction (906 cases), induction and intubation (201 cases) or for the conduct of the entire procedure

*Supplied through the courtesy of Parke, Davis and Company, Detroit, Michigan.

with or without nitrous oxide as the complementary agent (278 cases).

The patients varied from 3 to 80 years of age and included all degrees of surgical and anesthetic risks. Cases were taken at random and no attempt was made to choose any particular patient. The duration of anesthesia varied from five minutes to five hours. The surgery represented most procedures ordinarily performed in a fairly large general hospital.

The patients to be anesthetized with surital were premedicated in the usual manner. A barbiturate (usually nembutal or seconal) was given by mouth one and one-half to two hours before induction of anesthesia. One to one and one-half hours before induction demerol combined with scopolamine or atropine was given intramuscularly. Morphine was occasionally substituted for demerol. In emergency surgery the barbiturate was eliminated and the demerol-scopolamine combination was administered intravenously.

The drug was usually employed in concentrations of 0.2 per cent, 2½ per cent and 5 per cent. Occasionally 0.1 per cent and 2 per cent concentrations were used in the very young and very old. The 0.2 per cent concentration was generally used as a drip solution, the drug being dissolved in 5 per cent dextrose in distilled water. This is the technic we employ whenever an intravenous barbituric acid is to be used for any length of time for an anesthetic procedure in which nitrous oxide is the complementary anesthetic agent. The 2 per cent and 2½ per cent concentrations, used only for induction, were made by dissolving the drug in distilled water. This was followed usually by cyclopropane. The 5 per cent concentration of the agent was dissolved in distilled water and combined with a muscle relaxant, usually decamethonium bromide (C10), in the ratio of 0.4 Gm. of the barbiturate and 4 mg. of C10. This is the combination that we use when we utilize intravenous barbituric acids combined with muscle relaxants for endotracheal intubation.[11] In children under 8 years of age this concentration was halved. Following intubation nitrous oxide and ether or cyclopropane was used.

Use of Sodium Surital as an Induction Agent

Sodium surital was used alone as an induction agent in 906 cases. The 2 per cent concentration was given to 147 patients and the 2½ per cent concentration to 759 patients. A smooth, rapid induction is provided when doses of 100 to 300 mg. of sodium surital are given (chart 1).

Respiratory Depression. From 15 to 20 seconds following the injection of the drug there occurred a brief period of hyperpnea

CHART 1

Summary of Complications with Sodium Surital in the 2 and 2½% Concentrations

Age Groups	No. Pts.	No. of Pts. Surital		Surital Av. Amt.		Average Pulse Rate		Average Blood Pressure		Arrhythmias	Cough	Hiccough	Laryngospasm	Bronchospasm	Stridor
		2%	2.5%	2%	2.5%	Before	After	Before	After						
0-10	17	17 (1%)	0	95 (1%)	0	126	105	.....	.....	0	0	0	0	0	0
10-20	75	12	63	155	210	110	80	108/64	102/61	1	0	0	0	0	0
20-30	210	18	192	195	220	94	76	110/68	102/65	1	2	2	1	0	0
30-40	194	20	174	190	245	93	78	110/66	105/65	8	1	0	2	0	3
40-50	186	36	150	187	228	92	78	123/76	116/73	7	2	0	2	1	2
50-60	126	16	110	195	230	92	77	125/75	113/69	4	3	1	5	0	1
60±	98	28	70	170	200	91	70	137/80	105/70	2	4	0	2	1	3
—	906	147	759	..	..	..	..	..	..	23	12	3	12	2	9

followed usually by a somewhat longer period of hypopnea. Occasionally a brief apneic period lasting as a rule no longer than a few seconds was interspersed between the hyperpneic and hypopneic phases. Depression of respiration was not of any great significance in these groups and when present it was manifested mainly as a reduction in tidal exchange rather than in respiratory rate. The establishment and maintenance of inhalation anesthesia was then accomplished with ease.

Circulatory Depression. Hypotension was not significant. The blood pressure was decreased an average of 5 to 12 mm. Hg. Larger doses of the agent given rapidly produced the most marked (but usually transient) falls in blood pressure. The pulse rate usually was reduced. However, in a small percentage of the cases there was a slight increase. The reduction in rate for all cases averaged about 20 beats per minute.

Laryngospasm. This complication is perhaps the most feared and the most serious of all that occur during intravenous barbiturate anesthesia. In this series there were 12 instances, none of which could be classified as severe. All were treated successfully with oxygen and with pressure on the rebreathing bag. It was our impression that laryngospasm was less frequent and more benign than with other intravenous barbiturates in common use.

Bronchospasm. This complication was noted in only 2 patients and was only moderately severe and was self-limiting.

Cough and Hiccough. Coughing was present in 12 patients and was initiated in most instances by the presence of secretions or the use of an oralpharyngeal airway in very light anesthesia. Hiccoughing occurred in 3 individuals, was mild and of short duration.

Arrhythmias. In 23 patients the heart beat exhibited extrasystoles and/or pulsus bigeminus. All of these, with the exception of 2, occurred from 5 to 30 minutes after cyclopropane was administered. All resorted to a normal rhythm after lightening the anesthesia.

Use of Sodium Surital as a Maintenance Agent

The use of sodium surital in a 0.2 per cent solution in 278 cases showed a dosage range from 150 mg. for a 5 minute procedure to 1,950 mg. for surgery lasting 3 hours. The patient receiving the largest dose reacted to painful stimuli before leaving the operating table and answered questions 20 minutes after completion of surgery. One patient received 900 mg. of the agent within a 30-minute period and exhibited a pulsus bigeminus as the only complication which reverted spontaneously to a normal rhythm soon after the agent was discontinued. Induction was usually smooth and main-

CHART 2

Summary of Complications with Sodium Surital Used in a .2% Concentration

Age Group Years	Surital 0.2%		Av. Length Procedure Hrs.	Hiccough	Cough	Arrhythmia	Bronchospasm	Laryngospasm	Stridor	Average Change in		
	No. Pts.	Av. Amt. Given Mg.								Systolic	Diastolic	Pulse Rate
0-10	15	265	1.0	0	0	0	0	0	0	—10	—5	—15
10-20	28	585	1.4	0	0	1	0	0	0	—10	—6	—16
20-30	43	575	1.0	1	1	1	0	0	0	—10	—10	—10
30-40	84	615	1.2	1	2	7	1	2	4	—12	—6	—8
40-50	42	668	1.1	0	0	3	1	1	2	—14	—7	—9
50-60	32	524	1.2	0	1	1	2	2	2	—5	—8	—8
60±	34	528	1.1	0	1	2	1	1	2	—6	—5	—5
	278	530	1.14	2	5	15	5	6	10	—10	—5	—10

tenance of anesthesia with sodium surital and nitrous oxide was easily accomplished (chart 2).

Arrhythmias. The most common complication in this series was the presence of pulsus bigeminus or extrasystoles in 15 patients. Each occurred soon after a relatively large amount of the drug was given rapidly and each reverted to a normal rhythm when the rate of administration of the agent was reduced or discontinued entirely. In 3 patients arrhythmias could be produced and be made to disappear at will by increasing or decreasing the rate of administration of sodium surital.

Laryngospasm. This complication was seen in 6 patients, in 2 it was severe and in the other 4 it was of a moderate nature. Pressure on the rebreathing bag with the use of oxygen was all that was necessary to break the spasm. The offending stimulus, such as an airway or mucus, was of course removed prior to the oxygen therapy.

Bronchospasm. This annoying and serious complication was a factor in 5 cases. Not one could be considered as severe.

Cough and Hiccough. Coughing was present in 5 cases and was of short duration. Hiccoughs occurred in 2 cases and were mild and self-limited. These complications were never prolonged nor severe enough to play an important role in the procedure.

Stridor. The 10 patients showing this complication were victims of the placing of an oral airway in very light anesthesia or showed an abundance of secretions in the oral pharynx. When the offending stimulus was removed and the anesthesia deepened, the stridor disappeared.

Circulatory Depression. A slight reduction in the average blood pressure of from 5 to 14 mm. Hg. was seen in this series. There was also a decline in pulse rate an average of 5 to 16 per minute. In 6 patients the pulse rate dropped below 50 and in 3 of these a normal pulse rate did not reappear until two to three hours after surgery was completed. The blood pressure in these cases was only slightly affected.

Respiratory Depression. Depression of respiration here was not of great significance and was manifested mainly as a reduction in tidal volume rather than in respiratory rate. Muscular relaxation in this series was of about the same magnitude as that obtained with other intravenous barbituric acids.

Use of Sodium Surital with Decamethonium Bromide for Induction and Intubation

The use of sodium surital in conjunction with decamethonium

CHART 3

Summary of Complications Using Sodium Surital in a 5% Concentration in Combination with Decamethonium Bromide

Age Groups Years	Procedure	Total No.	Surital Mg. Av.	Syncurine Mg. Av.	Average Pulse Rate		Average Blood Pressure		Arrhythmias	Bronchospasm	Apneas		Hypopneas		Av. Time in Minutes to Intubate
					Before	After	Before	After			No.	Av. Time	No.	Av. Time	
0-10	ENT (18) Intra-abd. (2) Misc. (0)	20	110	1.1	130	110	100/65	110/70	0	0	10	3.5	15	5	2.8
10-20	ENT (13) Intra-abd. (0) Misc. (16)	29	280	2.8	106	90	106/60	112/75	0	1	9	5.0	12	5	3.0
20-30	ENT (8) Intrathor. (6) Intra-abd. (8) Misc. (12)	34	350	3.5	97	95	108/73	120/80	1	0	6	3.4	9	7	3.5
30-40	ENT (4) Intrathor. (6) Intra-abd. (15) Misc. (12)	37	345	3.3	96	95	110/68	126/80	0	0	9	4.2	17	8	4.1
40-50	ENT (3) Intrathor. (4) Intra-abd. (9) Misc. (15)	31	346	3.3	93	89	114/70	130/84	4	0	6	5.0	12	8	3.1

CHART 3 (*Continued*)

50-60	ENT (3) Intrathor. (4) Intra-abd. (17) Misc. (4)	28	337	3.25	93	84	125/76	138/87	1	2	6	5	15	7.5	3.4
60±	ENT (2) Intrathor. (6) Intra-abd. (10) Misc. (4)	22	260	2.6	81	87	118/70	142/90	5	0	3	8	10	9	2.9
		201							11	3	49		90		

CHART 4

Summary of Complications Using Spirothal

STB Concentration	Total Pts.	Hiccough	Bronchospasm	Cough	Nausea and Vomiting	Apnea	Muscular Tone Increased	Hypopnea	Stridor	Sneezing	Arrhythmias
0.2%	30	9	1	3	5	0	0	0	1	1	5
2.5%	48	8	2	5	10	6	4	2	4	0	2
5.0%	68	11	7	3	1	21	5	20	1	0	6
All Conc.	146	28	10	11	16	27	9	22	6	1	13

bromide (C10) for rapid intubation in 201 patients was very satisfactory (chart 3). For adults the average amount of the barbiturate necessary ranged from 280 to 350 mg. in combination with 2.8 to 3.5 mg. of C10. The average time to intubate ranged from 2.8 minutes for children to 4.1 minutes in the 30 to 40 age group. The cords are usually abducted and intubation is accomplished with ease. In only 2 cases were we unable to intubate the patient following the use of as much as 400 mg. of sodium surital in combination with 4 mg. of decamethonium bromide. Cyclopropane was resorted to and a successful intubation was accomplished within seven minutes of the time of onset of administration of the barbiturate.

Respiratory Depression. Apnea followed intubation in 46 patients and lasted as long as 20 minutes. The average apneic period was about five minutes. Hypopnea was a complication in 90 cases and lasted as long as 15 minutes with an average of about seven minutes.

Circulatory System. Following this method of intubation the pulse rate decreased an average of about 10 per minute. This was not a consistent finding for in a fairly large percentage of the cases the pulse rate actually increased. The blood pressure almost invariably shows an increase and in all cases in this series there was an average increase of about 20 mm. Hg. In one 41 year old patient the blood changed from 110/60 before onset of induction to 200/120 (three minutes later) following intubation. We have had no apparent ill effects from these blood pressure phenomena.

Arrhythmias. Extrasystoles and pulsus bigeminus occurred in 11 cases in this series. All were of short duration and were self-limited.

Bronchospasm. This complication was seen in only 3 cases and was of moderate severity.

Conclusions

In this clinical study of surital sodium the most striking feature is the similarity of this drug to pentothal. However, the incidence, the duration, and the severity of laryngospasm were somewhat less with surital than that experienced with pentothal. The frequency and duration of apnea following the use of this new agent in combination with decamethonium bromide were less than when pentothal was used in the same manner. With these two exceptions it is doubtful whether one could differentiate between the two drugs solely on the basis of their action.

Most barbituric acid derivatives now in medical use are disubstitution products in the 5-position. Dox and Yoder[12,13] in 1921 prepared spiro-cyclobutane barbituric acid and spiro-cyclohexane barbituric acid by the formation of an alicyclic ring on the 5-carbon

atom. The latter C atom becomes common to both the alicyclic and pyrimidine rings. These workers, however, did not arrive at any active compounds.

In an effort to develop newer and possibly a better type of barbiturate suitable for intravenous use, the organic chemical division of the Lilly Research Laboratories synthesized a large number of derivatives of spirobarbituric acid and spirothiobarbituric acid. Swanson, Mueller, Henderson and Chen[14] reported on 50 of these compounds and found that four of them showed some promise. One referred to formerly as spirothiobarbituric acid 03620 and more recently named spirothal* has been studied by us. One hundred and forty-six cases are included in this group.

The same technique was employed here as was used with surital sodium. The ages ranged from 3 to 82 with about an equal number of males and females (chart 4).

Complications

Hiccough and Cough. In this series there were 28, or 19 per cent, cases of hiccough and 11, or 8 per cent cases of coughing. When these complications appeared they occurred within a few seconds after the drug was administered and persisted usually for from 1 to 10 minutes or until the drug was discontinued. In one instance the hiccoughs were present for 20 minutes.

Nausea and Vomiting. This was the second most common complication where the 0.2 per cent and 2.5 per cent concentration was utilized and occurred in 16 cases, or 11 per cent. In 4 of these vomiting took place within one minute of the beginning of induction and in the remainder it occurred at the termination of the procedure. These patients had received atropine alone or demerol and scopolamine as premedication and received spirothal alone or with nitrous oxide.

Bronchospasm. This was noted in 10 cases but did not prove to be severe at any time.

Arrhythmias. Extrasystoles and pulsus bigeminus occurred in 13 patients, and all reverted to a normal rhythm after slowing the administration of the agent or stopping it entirely.

Respiratory Depression. Apnea was a major complication in 27 patients with 21 of these in the series receiving the 5 per cent concentration of spirothal in combination with C10. Also in this group were 22 cases of hypopnea.

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*Supplied through the courtesy of Eli Lilly and Company.

Circulatory Changes. The blood pressure changes were not significant when spirothal was used alone. There was generally a drop of 10 to 20 mm. Hg. in both systolic and diastolic pressures. The greatest drop in this series was 36 mm. Hg. systolic and 20 mm. Hg. diastolic. Using a 5 per cent concentration combined with C10 the first 200 to 250 mg. of spirothal produced a drop of 10 to 20 mm. Hg. but after an additional amount of the drugs sufficient to do endotracheal intubation was given a rise in blood pressure usually occurred which varied from 10 mm. Hg. to as much as 120 mm. Hg. systolic and diastolic, with the average being from 50 to 70 mm. Hg. This rise was sustained for 10 to 20 minutes and then dropped gradually to the patient's preinduction level. Such a rise in blood pressure could not be obtained with either of the agents alone, nor was it observed when decamethonium bromide was used in combination with other barbituric acids.

Muscular Relaxation. It was not uncommon for many of the patients to have an increased muscle tone within two to four minutes after the drug was injected. Purposeless movements similar to those seen with evipal sodium were observed. In one patient in whom we attempted endotracheal intubation under the influence of 5 per cent spirothal alone it was practically impossible to open the mouth even though 0.5 Gm. of the drug was given within one minute's time.

Other Complications. Sneezing was so persistent in one patient that the administration of the agent had to be discontinued. This was controlled within a few minutes with cyclopropane. Stridor was of minor importance.

Summary

In this small series of 146 cases in which spirothal was given in either a 0.2 per cent, 2.5 per cent or 5 per cent concentration the frequency and severity of nausea, vomiting, coughing, hiccoughing, apneas, arrhythmias, and blood pressure phenomena, were greater than with other intravenous barbituric acid derivatives in current use.

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RECONSTRUCTIVE SURGERY OF THE LIP REGION

W. S. Flanagin, M.D.*
Augusta

A GREAT variety of deformities occur in the vicinity of the lips and in almost every case there are many methods of repair from which one may choose. Every effort is made to restore the affected part to normal appearance and function and to retain the delicate kinetic balance of this region.

The facial muscles converging upon the oral fissure make the mouth an ever changing focus of expression. Its function and appearance determine largely the character of the face. Any deformity, lack of symmetry or limitation of motion is immediately discerned. The lips are draped in front of the teeth, free to move in any direction, because of their distance from bony attachment.

Whenever possible nature heals with contracture, as is seen following a deep burn over a flexion crease. Due to the elastic soft tissue construction of the lips a similar situation exists and, following injury, there is no resistance to this pattern to contract and distort any part of the mouth that may be involved.

Occasionally there is seen a minor defect of the upper lip with a redundant vermilion and asymmetry resulting from a transverse laceration of the lining near the lip border. The scar contracts and becomes fixed to the subcutaneous tissue. The deformity is exaggerated upon smiling because the affected segment is unable to stretch out from lack of normal elastic mucosa.

This is repaired by incising along the scarred mucosa and making a small Z-plasty. By this maneuver the fixed points are spread apart and the scar is staggered, thus preventing a second contracture on completion of healing (fig. 1).

Deep lacerations passing back from the corner of the mouth are usually in a poor direction for kind healing without contracture because they cross the lines of skin tension. To offset and minimize this tendency a straight-line closure must be avoided by cutting many small Z's in the skin, transposing the flaps and suturing. In closing a lateral fissure the mucosa, muscle and skin should be sutured at different levels for the best function and appearance (figs. 2 and 3).

Often a fistula of the cheek is repaired by bringing in flaps from a distance after many operative sessions. A method is presented here whereby two flaps are utilized to close a fistula in one operation

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From the Department of Plastic Surgery, Medical College of Georgia.
*Associate Professor of Plastic Surgery.

without increased facial deformity. It is a rule that all cavities must be lined to prevent chronic inflammation and delayed healing. A small hinge-flap is turned back from one side of the opening to serve as the lining and a second flap is turned down to cover all raw surfaces. The cornified epithelium of a flap or a free graft is a satisfactory substitute for the oral mucosa (fig. 4).

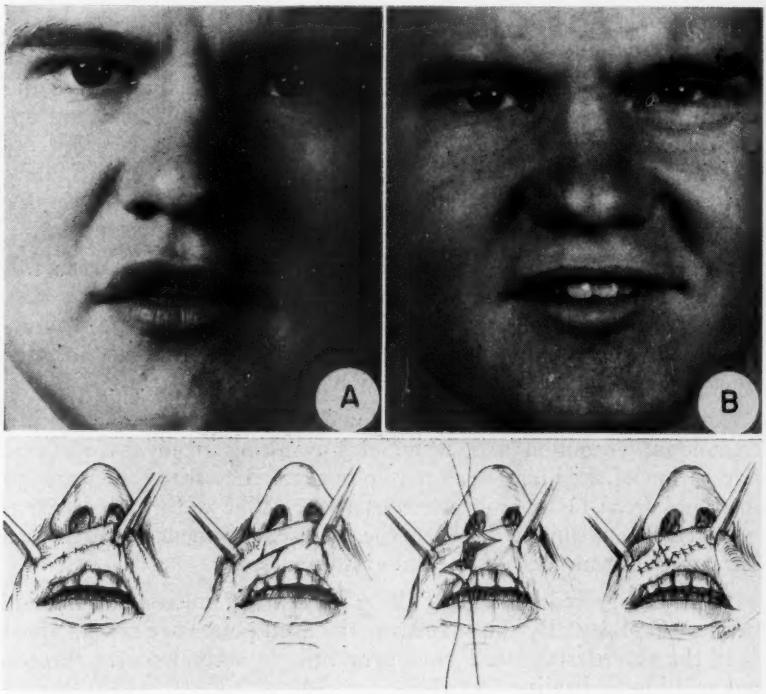

Fig. 1 a. A defect on the right side of the upper lip that is exaggerated on smiling due to contracture following traumatic transverse laceration of the mucosa. Asymmetry and vermilion redundancy can be seen. b. Appearance after repair by the method depicted in the drawings below. The scar was incised, a small Z cut and the flaps transposed, thereby preventing a secondary contracture on completion of healing.

In the repair of any defect every effort should be exhausted to use tissue adjacent to the defect. Sometimes it seems that we lose sight of this principle and become engrossed in mobilization of large tube pedicles when a good reconstruction could be obtained with fewer operative stages by using the available adjacent tissue.

A defect of the upper lip near the nose that cannot be repaired without shifting tissue may entail the elevation of a flap from the

side of the mouth and rotation of it into the defect. This may be easily done in an elderly individual whose skin is relaxed with a minimum of scarring and deformity at the donor site. It often is not necessary to smooth out the "dog-ear" (fig. 5).

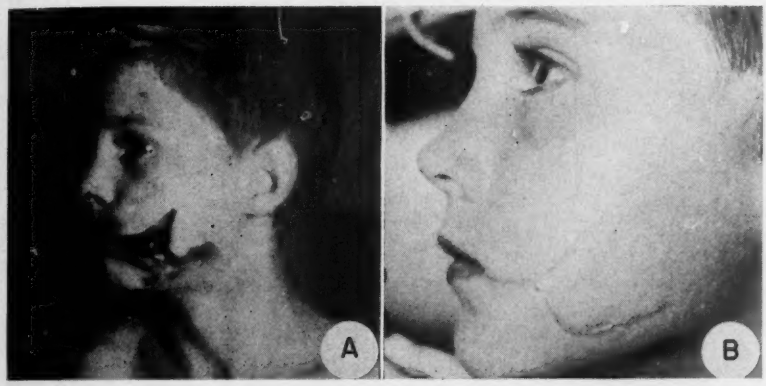

Fig. 2 a. Preoperative view of a full thickness cheek tear from the corner of mouth to the ramus of mandible created by the handle of a passing car. b. Appearance after closure.

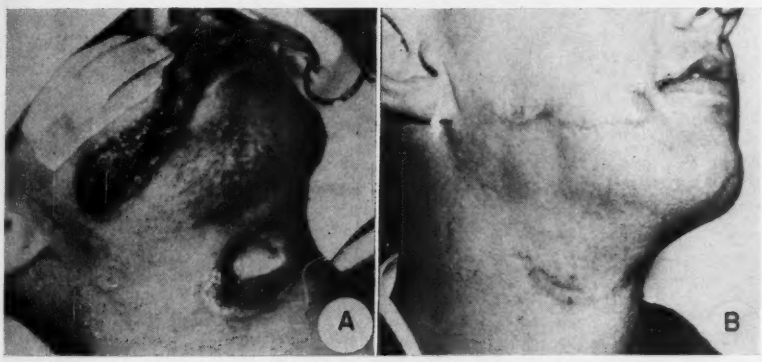

Fig. 3 a. Preoperative view of mouth fissure resulting from an electric burn. b. Postoperative. After closure of neck and cheek defect by contiguous flaps. The fissure was closed by suturing the mucosa, muscle and skin at different levels so as to stagger the scar.

These rotated flaps constitute one of the ideal methods of repair of defects from the standpoint of tissue cost, time used and cosmetic results. It may be difficult to visualize the reconstruction by this means and imagination and experience are helpful. To get a safe transfer with complete survival the length of the flap should never exceed its width by more than 3 to 1. The plan of reconstruction

should be slow and deliberate for after its execution it is impossible to turn the clock back and begin anew.

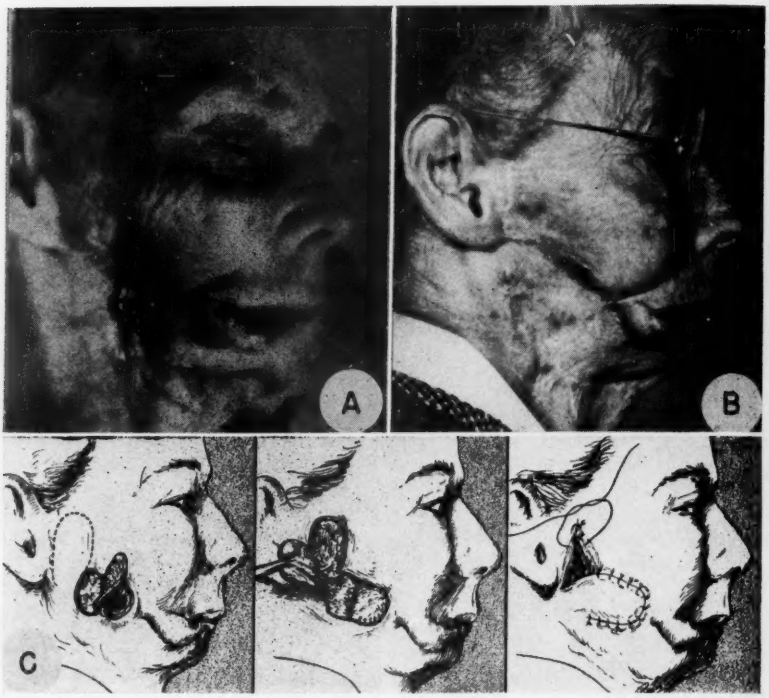

Fig. 4 a. Fistula in cheek. b. After closure of fistula in one operation. c. Drawings to show method of repair. A hinge-flap was turned back to line the fistula. A second flap was then elevated from in front of the ear and rotated to resurface the denuded area.

Some combination of a harelip or cleft palate is the most frequent congenital defect of the face, occurring in some 1 in 800 births. There is lack of fusion of the defective bony and soft parts by the ninth week in utero. Double clefts are most difficult to repair. They constantly have a short columella and the premaxilla may protrude in advance of the arch of the alveolus. The harelips are repaired early but the palatal defects are delayed until the child is some two years of age (figs. 6 and 7).

Very often an individual who has had an adequate repair of an old double harelip in infancy may seek relief upon reaching maturity from the typical facial stigma of such a defect. They are overwhelmed by an inferiority complex and are crippled in a true sense. On analysis such a lip is usually short, tight and scarred. The nos-

trils are usually not symmetrical and are of poor shape due to the tip of the nose being held too close to the face by the short columella. On profile the retruded tip of the nose is quickly detected. There

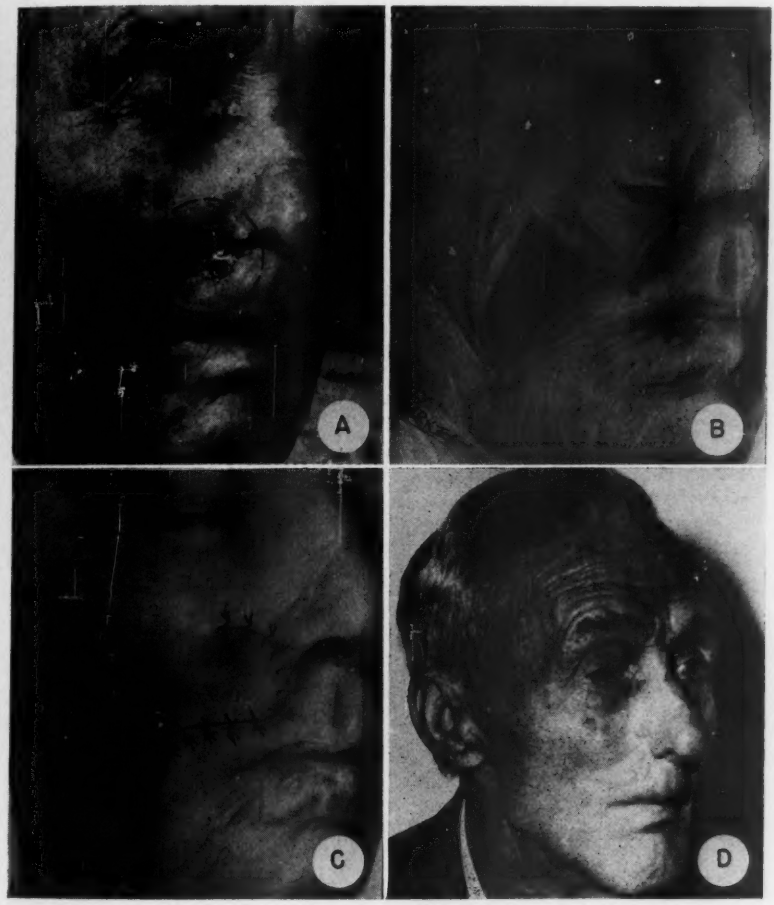

Fig. 5 a. Malignancy with ulceration in right nose-lip region. Excision indicated by broken line includes all structures to mucosa. b. A flap was marked to the right of the mouth, elevated, rotated and sutured into the defect as indicated by the drawing. c. Sutures in situ. d. Final appearance showing good cosmesis and no deformity at the donor site.

is often a noticeable lack of tissue in the center of the upper lip. The lower lip protrudes in advance of the upper lip—the reverse of normal. From some distance one can diagnose the condition.

The problem is how to restore a normal profile and frontal ap-

pearance with the least number of operations. All objectives can be accomplished by advancing the lip onto the columella, thereby lengthening the tip of the nose and giving it a normal dorsal curve.

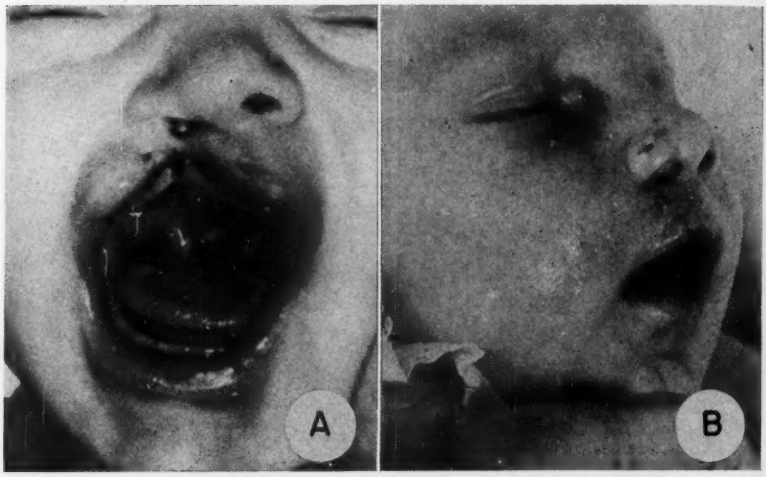

Fig. 6 a. An incomplete right-sided harelip with associated slumped nostril. A cleft of the palate can be seen. b. Six days after repair of the harelip by the Hagedorn method.

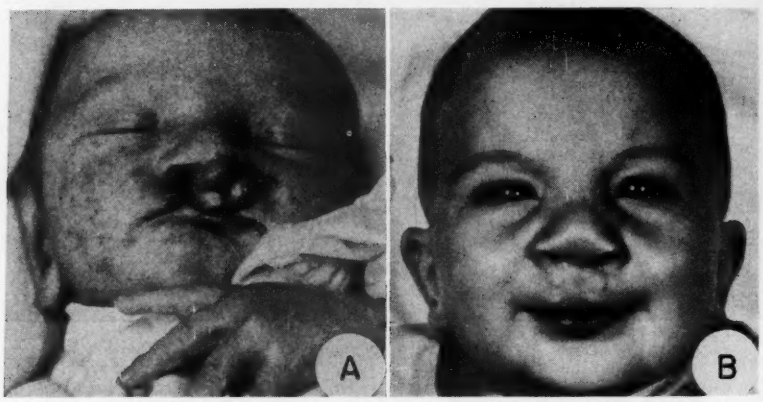

Fig. 7 a. A complete double harelip. The premaxilla protrudes beyond the arch of the alveolus. b. After the premaxilla was set back and the lip repaired.

Then a wedge full-thickness flap is rotated out of the lower lip 180 degrees with a single narrow attachment along one side carrying the inferior labial artery for nutrition. After the upper lip has been opened and the scar excised, this wedge from the lower lip is at-

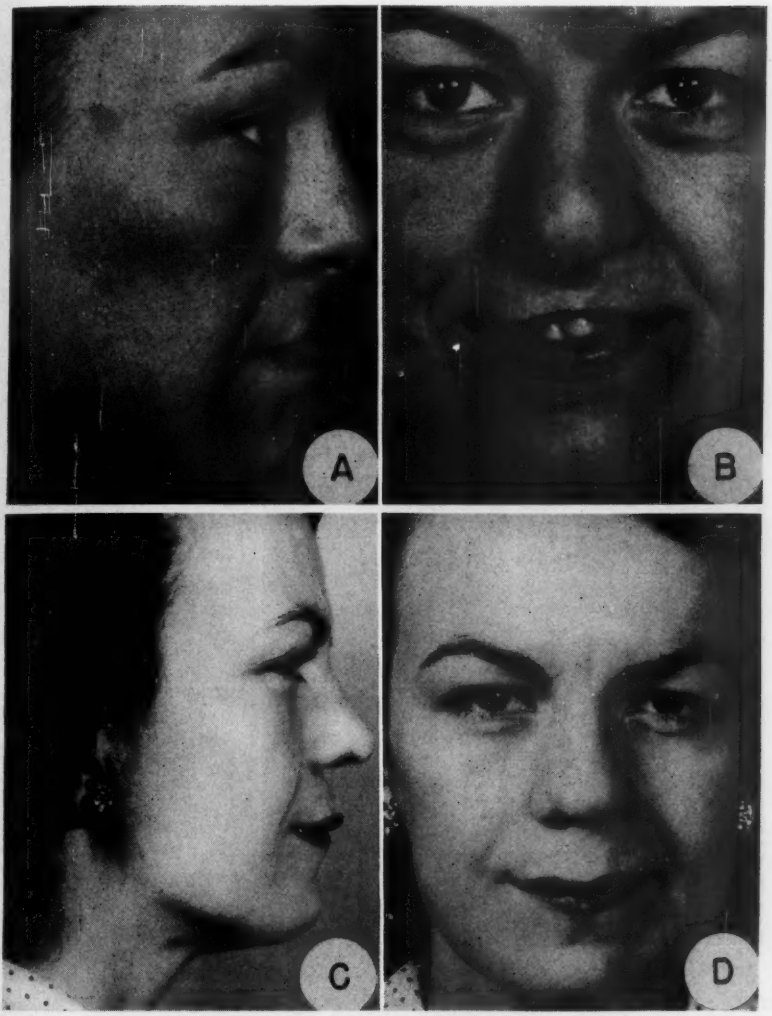

Fig. 8 a. Right side view of a markedly deformed upper lip as a result of a double harelip. The tip of the nose is retruded due to the short nasal columella. The upper lip is too short and tight with much scarring in the center. The lower lip protrudes beyond the upper lip—the reverse of normal. b. The scarring is seen and the short upper lip fails to cover the crooked teeth. This condition can be easily diagnosed from a distance. c. After repair. The center of the upper lip was advanced to lengthen the columella of the nose, thereby correcting the retrusion. Flap from lower lip supplies necessary tissue for large defect of upper lip, restoring normal relationship to lower lip. d. Front view to show the full thickness flap that was switched from the lower lip into the defect of the upper lip. Marked improvement in appearance is seen, with the upper lip covering the teeth and restoration of the profile lines to normal.

tached and sutured into the defect. In some two weeks the pedicle is detached and its edges trimmed and sutured (fig. 8).

Defects of the lower lip are much more common than those of the upper lip. Due to the elasticity of the lip it is possible to excise a malignancy along with an adequate margin of normal tissue and still close the defect by approximation with a pleasing cosmetic result. Vertical defects up to one-third the width of the lip may be handled in this manner. Should the lip protrude excessively following this closure some other method of repair is indicated. Or it may be left tight to see just how much relaxation will follow in several months after the tissue has softened. If needed, at that time a mouth widening procedure may be done.

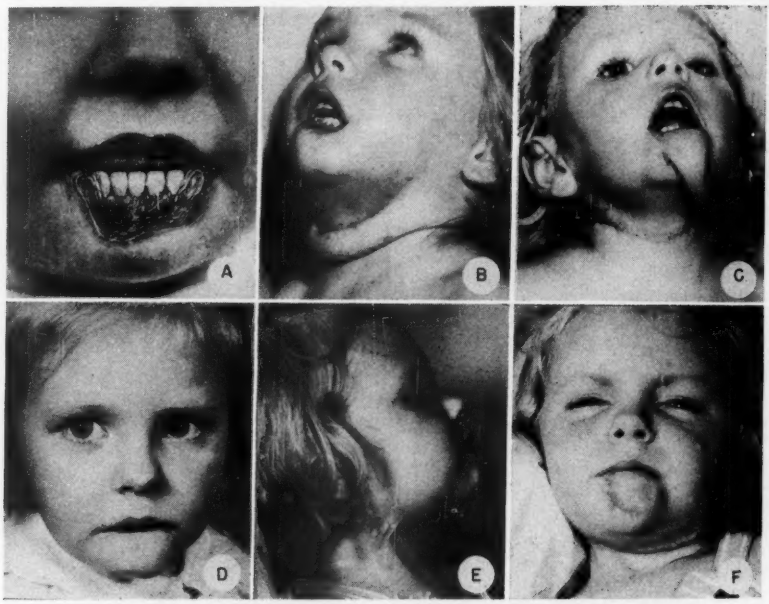

Fig. 9 a. Traumatic void of lower lip. b. A transverse cervical skin tube has been constructed. c. The tube is attached to the defect. d. The tube has been detached. e. Profile appearance after final plastic operation when excess fat was removed. f. Final result—front view.

Larger defects up to one-half the length of the lip may be effectively repaired by turning an artery Abbe flap from the upper lip. This is a good method but a secondary revision at the corner of the mouth to regain symmetry must be done later.

In losses of the vermilion border along most of a lip the buccal

mucosa is undermined and advanced forward to cover the denuded area.

For a complete void of the lower lip along with loss of tissue from the chin the modified Dieffenbach procedure furnishes good closure. Here large cheek flaps are mobilized and advanced under the upper lip. This is an extensive procedure.

Distant tube flaps may be constructed and brought in to fill a void of the lower lip. This requires several operations but the appearance is satisfactory. A red vermilion must be grafted with mucosa or tattooed on to complete the repair (fig. 9).

SUMMARY

An assortment of congenital and acquired defects of the lips occur. Due to the increased incidence of malignancy of the lower lip large defects here are more common than those of the upper lip.

It takes an exceptionally well adjusted individual to tolerate disfigurement in such a prominent location without a great deal of psychic trauma.

The surgical approach in every case presents varying problems and good results are dependent upon patience, time and adherence to sound surgical principles.

Note: The author is indebted to Mr. Orville A. Parkes and Staff of the Department of Medical Illustration for the drawings, photographs and helpful suggestions.

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PEDUNCULATED SUBMUCOUS MYOMAS OF THE UTERUS

GUY L. CALK, M.D.*
RICHARD TORPIN, M.D.**
Augusta

THIS paper is a report of 24 cases of pedunculated submucous myoma encountered on the Gynecological service of the University Hospital, Augusta, Georgia, over a 16 year period. Twenty of these cases were observed at the University Hospital while 4 were seen by one of us in a six months' period at the Macon General Hospital in Macon, Georgia.

Literature on the subject of submucous myomata is rather scanty but mention is made in most of the standard textbooks on Gynecology, particularly those on operative Gynecology. Especially good is the work of H. A. Kelly and T. S. Cullen.[1] Since the journalistic literature is meager, it is our purpose to present herein 12 cases of pedunculated submucous myomata and give a simple method of treating this condition.

Incidence:

Frank[2] mentions only one pedunculated submucous fibromyoma in a study of 916 cases of fibromyomata. Gainey and Keeler[3] reported 4 cases of submucous fibromyomata discovered in the puerperal period following full term deliveries.

The instrument used in most of these cases is composed of the parts illustrated. The snare is of narrow stainless steel plate, 12 in. by ½ in. by 3/16 in., and may be fabricated in any workshop. The two holes as illustrated are countersunk on each side. The hole near the end is important in that it allows one-fourth inch or more of the steel plate to act as a fulcrum to hold the uterine wall distally away from the wire as it cuts the pedicle of the tumor close to the myoma. This close cutting mechanism is of importance in that it obviates the danger of opening into the peritoneal cavity, should there be invaginating action of the pedicle upon the uterine wall. This crushing procedure as the pedicle is cut is of hemostatic value and in most cases there was little subsequent bleeding and the pedicle retracts so that immediately it may be impossible to palpate its location in the uterine wall. In most cases, however, a sterile pack is introduced firmly.

It is important that heavy piano or steel wire be used, No. 13

From the Department of Obstetrics and Gynecology, Medical College of Georgia.
*Resident, Obstetrics and Gynecology.
**Professor of Obstetrics and Gynecology.

being very satisfactory. A pair of mechanic's pliers with wire cutting component is of value in cutting the wire from the roll and it is possible to use the pliers to wind the ends of the wire in snaring off the tumor pedicle. The T type rod with two small holes is more convenient and efficient, inasmuch as the force necessary to sever large pedicles is considerable.

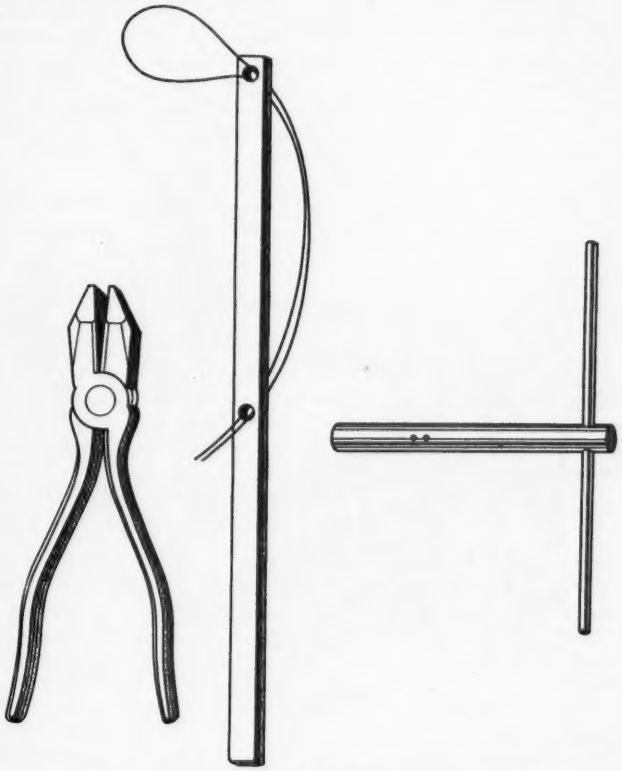

Fig. 1. Snare and accessories for removal of submucous pedunculated myomas of the uterus.

We believe that since there is danger of virulent infection with many of these pedunculated tumors, often with necrotic surfaces, the minimum effective operative therapy is indicated. Anemia is usually quite severe and this adds to the danger. Today this may be reduced with immediate preoperative transfusions.

Case Reports

Case 1. A. P., 27 year old colored female, was first seen in the clinic in

March 1950 because of menorrhagia. She was admitted to the hospital where she was found to have an hemoglobin determination of 6.0 Gm. She was given replacement transfusions and a dilatation and curettage was performed with slight cystic glandular hyperplasia of the endometrium being found on pathological examination. She was dismissed from the hospital and had regular periods but her periods were characterized by increased amount of blood loss and severe cramps throughout her menses. On Aug. 3, 1950, she began menstruating with heavy flow at first and severe cramps which persisted along

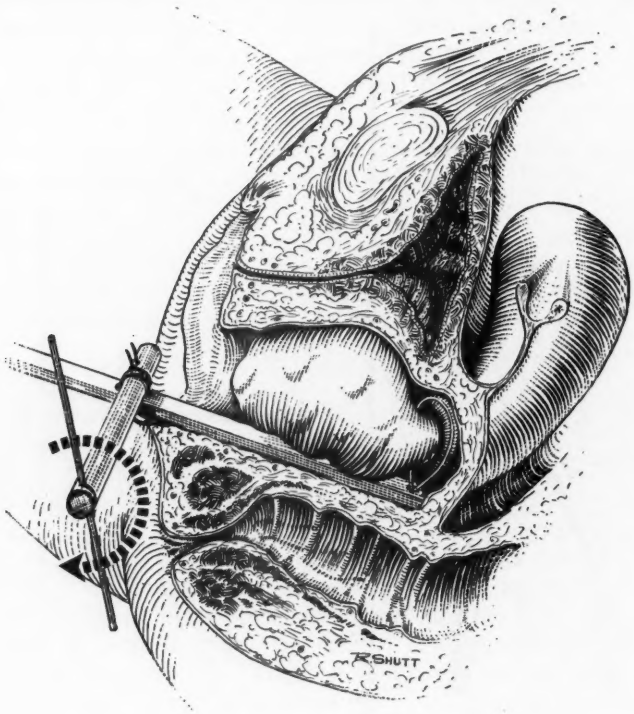

Fig. 2. Snare in operation.

with slight bleeding which had a foul odor until Aug. 31, 1950, when she was again admitted to the hospital. On admission this second time she was found to have an hemoglobin determination of only 4.0 Gm. She was given transfusions again and on Sept. 7, 1950, a second dilatation and curettage was performed. The endometrial scrappings revealed only resting glands in a vascular stroma. Vaginal bleeding ceased for three weeks but on Sept. 28, 1950, she reported at the clinic complaining of laborlike pains in her lower abdomen and profuse vaginal bleeding. Examination revealed a submucous pedunculated fibromyoma approximately 2 cm. in diameter hanging by a small pedicle from within the cervical canal. Hemoglobin determination revealed

8.0 Gm. and transfusions were again given. She was taken to the operating room where the submucous polypoid tumor was snared, the pedicle being cauterized and the uterine cavity packed. The pack was removed 24 hours postoperatively and her convalescence was uneventful. Pathological examination of the excised specimen revealed a polypoid mass 2.5 cm. in diameter, the cut surface showing light gray fascicular appearance. Microscopic sections revealed myomatous structure with marginal reactive changes.

CASE 2. E. S., 29 year old nulligravid colored female, was admitted to the hospital Nov. 14, 1950, and stated that since March 1950 she had had frequent episodes of profuse vaginal bleeding associated with severe lower abdominal cramps. On examination the patient was an emaciated and anemic colored female with blood pressure of 98/40. The heart was enlarged to percussion and Grade 2 systolic murmur was audible at the apex. Pelvic examination revealed vaginal bleeding with an offensive odor. The vaginal vault was filled by a firm roughly circular mass approximately 8 cm. in diameter behind which the examining finger could palpate a cervix dilated 2 cm. and an attenuated pedicle attached to the tumor mass and arising from within the uterine cavity. The hemoglobin determination was found to be less than 2 Gm. so blood transfusions were begun immediately. The patient was taken to the operating room and under local anesthesia (pudendal block), the wire was fitted about the tumor in the vaginal vault and the tumor excised by simply snaring the pedicle. After removal of the tumor, the pedicle had retracted so that it could not be visualized. Then the uterine cavity was gently probed and a pack inserted. The patient was given replacement transfusions, the pack removed in 24 hours postoperatively, and convalescence was uneventful. Pathological examination of the specimen revealed a sharply circumscribed mass 7.0 cm. in the greatest diameter showing a glistening gray fascicular cut surface. Microscopic sections revealed closely packed smooth muscle bundles with focal areas of mucoid degeneration.

CASE 3. M. S., 37 year old colored female, was admitted to the hospital on Dec. 16, 1950, with a history of prolonged and painful periods for 13 months. Eight days prior to admission she began to menstruate profusely and had laborlike lower abdominal cramps. The bleeding had been so profuse that she had become quite weakened. She had had three full term pregnancies, her youngest child being 14 years of age. The patient was an anemic debilitated individual who exhibited pronounced weakness. A Grade 2 systolic murmur was audible over the precordium. Pelvic examination revealed profuse dark vaginal bleeding. The upper vaginal vault was filled with a round firm tumor mass approximately 4 cm. in diameter. The tumor was suspended by an attenuated pedicle arising from within the uterine cavity and passing through the cervix which was dilated 2 cm. The fundus of the uterus was enlarged by multiple nodular tumors to the level of the umbilicus. Hemoglobin determination on admission was 8.3 Gm. Two whole blood transfusions were given and the following morning the patient was taken to the operating room where the pedunculated submucous fibromyoma was easily snared under general anesthesia. The pedicle was visualized but no bleeding was noted. The uterine cavity was packed, however, and the patient left the operating room in good condition. The pack was removed 24 hours postoperatively and the convalescence was complicated only by a mild cystitis. The pathological examination revealed a fibroelastic lobulated mass 3 cm. in diameter, the cut surface revealed a glistening light gray appearance. The patient was readmitted to

the hospital in February 1951 and a total abdominal hysterectomy was performed.

CASE 4. L. M. W., 33 year old colored female, was admitted to the hospital on Nov. 28, 1950, and related that she had had vaginal bleeding since August 1950. Her bleeding had been continuous but at times was much more profuse. She felt that she had aborted in September 1950 when she bled profusely with passage of several large clots and had cramping pains in her lower abdomen. She had been pregnant on three previous occasions but all pregnancies had resulted in abortions at two or three months' gestation. On examination she was found to have a soft blowing systolic murmur over the entire precordiun. Vaginal examination revealed slight bleeding with an offensive odor. The upper vaginal vault contained a circular firm mass approximately 5 cm. in diameter with a necrotic purplish surface. The mass was connected to a pedicle protruding through the cervix. The fundus of the uterus was enlarged by multiple fibromyomata to the umbilicus. The hemoglobin was determined to be 9.4 Gm. A blood transfusion was given and patient taken to the operating room where the pedunculated submucous fibroid was pulled through a loop of wire and the pedicle severed. The uterine cavity was packed when slight bleeding resulted following severance of the pedicle. The pack was removed 24 hours postoperatively and the patient had a serosanguineous discharge for 5 days. Pathological examination of the specimen revealed a firm polypoid mass measuring 4.5 cm. by 4 cm. by 3 cm. with a purplish surface discoloration. The cut surface revealed a characteristic glistening light gray fascicular appearance of fibromyoma. Microscopic section revealed no evidence of malignancy. The patient was readmitted to the hospital in January 1951 and total abdominal hysterectomy was performed.

CASE 5. E. M., 44 year old colored female, admitted Mar. 12, 1950, because of excessive menstruation of 15 months' duration. She related that her periods were always regular prior to onset of excessive bleeding at the time of her menses and she began noticing passage of clots and cramping. She had had two pregnancies with living children 22 and 15 years of age. On examination she was obese and appeared anemic. The pelvic examination revealed a tumor mass 3 cm. in diameter in the vaginal vault and suspended from within the uterus by a small pedicle passing through the cervix. The hemoglobin level was determined to be 7.5 Gm. and she was given two whole blood transfusions. She was taken to the operating room the following day and the pedicle of the protruding fibroid was easily severed with the wire loop. The pedicle retracted into the uterus and the cavity was packed. The uterine pack was removed 24 hours postoperatively and the convalescence was uncomplicated. Pathological examination revealed a detached pedunculated fibromyoma 3.5 cm. in diameter. The surface was in part covered with extremely anaplastic squamous epithelium representing a preinvasive carcinoma. At follow-up clinic 6 weeks postoperatively the patient was found to have a normal pelvis on examination and Papanicolaou smears were reported negative.

CASE 6. Mrs. A. W., 40 year old white female, admitted to the hospital Feb. 9, 1943. She related that her periods had previously been regular but with onset of menses eight days prior to admission she had severe cramps and profuse bleeding which lessened in amount daily until the day prior to admission when she was suddenly relieved of pain but had profuse bleeding. She had been pregnant three times with all pregnancies resulting in full term

living children with ages of 18, 12, and 3. She was an obese female in no apparent distress with a soft systolic murmur audible over the mitral area. Pelvic examination revealed a hard round mass approximately 5 cm. in diameter adjacent to the cervix which was dilated approximately 4 cm. The hemoglobin determination was 9.0 Gm. and a blood transfusion was given. Vaginal bleeding became excessive and three additional transfusions were administered. She was then taken to the operating room and a mass was found to be attached to a broad pedicle arising from the posterior lip of the cervix. The wire loop was slipped around the fibroid and the pedicle snared, leaving a raw area 1 cm. in diameter on the posterior cervical lip. Two interrupted catgut sutures closed the raw surface. The convalescence was uneventful and she returned three months following the vaginal myomectomy and underwent total abdominal hysterectomy without complications.

CASE 7. Mrs. A. T., 38 year old white female, admitted to the hospital May 22, 1940, because of severe vaginal bleeding which had commenced four weeks prior to admission. She stated that she had noticed for the past several months that her periods were more prolonged and profuse with slight cramping. Her regular menses had begun four weeks previously with severe bleeding and cramps lasting two weeks but had spotted each day until admission. She had had three full term pregnancies with living children, the youngest being 16 years of age. Pelvic examination revealed a lemon sized firm mass free in the vagina and suspended from within a patulous cervix by a thin pedicle arising from the right lateral wall of the uterus. The hemoglobin level was found to be 9.5 Gm. She was given a blood transfusion and the following morning the pedunculated fibroid was simply severed with the wire loop. The pedicle was cauterized with the electrocautery. The patulous cervix admitted the finger and exploration of the uterine cavity revealed no abnormality. The uterine cavity was then packed to insure against further bleeding. She was dismissed the day following operation after the pack was removed. The pathologic report was received after the patient was dismissed and revealed a spherical liomyosarcoma 5 cm. in diameter, covered in part with decidual-like endometrium and in part with infected granulation tissue; dilatation of the vessels at the base with thromboses of some. The patient was contacted but refused to return until six months following the vaginal myomectomy. Total abdominal hysterectomy was performed and no malignancy was demonstrable in the excised uterus.

CASE 8. E. M., 40 year old colored female, admitted to the hospital Mar. 19, 1949, because of urinary retention. She had experienced difficulty on urination for two years with frequency at intervals of 10 minutes at times. She stated that she had not urinated in the past 36 hours. She had been aware of fullness in her vagina several months and this had prevented intercourse. Her last regular menses had been one year previously and she had noticed no bleeding until two weeks prior to admission when spotting only was noted. She had been pregnant 22 years previously but the pregnancy terminated in an abortion at three months gestation. On examination she was obese and obviously in considerable pain. Her abdomen was distended and quite tender in the lower quadrants. She was catheterized and 1,200 cc. of cloudy urine was obtained. When the catheterization was performed a necrotic mass was noted at the introitus. The odor was very offensive. Further pelvic examination revealed the vagina to be markedly distended by a large firm mass some 10 cm. in diameter around which the examining finger could not explore. The urine

contained numerous white blood cells and the hemoglobin determination revealed 6.5 Gm. Whole blood transfusions were begun immediately and the patient was transferred to the operating room. Under general anesthesia the tumor prevented palpation of the cervix and made use of the snare unsafe. An episiotomy was performed and the fibroid was delivered with Simpson forceps. The pedicle was then easily visualized and ligation with severance of the pedicle was performed. The episiotomy was repaired and vaginal vault packed. The patient was unable to urinate voluntarily for three days postoperatively. The vaginal pack was removed and the episiotomy site was slightly infected and had broken down superficially. Hot packs were applied to the perineum and the hospital course was otherwise not unusual. Pathological examination of the specimen revealed a submucous fibromyoma measuring 9.5 cm. with a necrotic surface and composed of fibromuscular tissue. This patient was not seen in the follow-up clinic and has not been contacted as yet.

Case 9. E. M. B., 43 year old colored female, admitted to the hospital May 29, 1946. She stated that four years previously she had noticed a lump in her right lower quadrant which had increased progressively in size until presently it was the size of a grapefruit. Her last three menstrual periods had been characterized by excessive bleeding and cramping. Her last menses had begun four days prior to admission and the bleeding was so excessive that she was weakened but she experienced no pain with this period. She had had five pregnancies but only two had resulted in full term children whose present ages were 28 and 17 years. There were three abortions at four or five months' gestation between the two term pregnancies. Examination revealed a medium sized Negress who appeared quite anemic with a pulse rate of 120. A blowing systolic murmur was heard over the entire precordium. A firm nodular mass was palpable arising from the pelvis and extending slightly above the umbilicus on the right. Her hemoglobin determination was found to be only 3.2 Gm. Shortly after admission a pelvic examination was being done and the patient hemorrhaged profusely and blood pressure fell to 70/0. She was rushed to the operating room where blood transfusions were given and pelvic examination revealed a large mass completely filling the vagina and obscuring palpation of the cervix. The vagina was packed around the mass but this did not control the bleeding. The following morning after blood had been given the patient was returned to the operating room in a remarkably improved condition and the tumor was pulled down with tenaculae and the wire loop slipped around the fibroid. The pedicle was severed by simply tightening the wire and the tumor was removed. Inspection revealed no bleeding but the uterine cavity was packed and the patient had an uneventful hospital course. The pathological department reported a pedunculated submucous fibromyoma 10 cm. in diameter with ulceration of the surface. Wall of myometrium some 1 cm. in thickness surrounds the severed base. This patient was not seen again following dismissal from the hospital.

Case 10. H. J. M., 33 year old colored female, admitted to the hospital on Oct. 21, 1936, with a history of prolonged periods for past six years. About twice a year she was forced to bed because of excessive bleeding, but the past year she had had several episodes of profuse bleeding with cramping, lower abdominal pain during the active bleeding. Her last menses had begun two weeks prior to admission and was still present. She had had one pregnancy the previous year but it had terminated in abortion at three months' gestation. She was an obese Negress in no distress but appeared quite anemic. Pelvic

examination revealed a mass approximately 5 cm. in diameter in the upper vaginal vault and attached to an attenuated pedicle arising from above the dilated cervix. The fundus of the uterus was enlarged to size of an orange by multiple nodular masses. Hemoglobin determination was 6.2 Gm. She was given two whole blood transfusions and reacted rather severely to the second one with vascular collapse and anuria for two days. At the end of 2 weeks she was found to have a P.S.P. excretion of 55 per cent. She was then taken to the operating room where the pedunculated submucous fibromyoma was snared under local anesthesia. The pedicle was cauterized and convalescence was uneventful. Pathological examination revealed detached fibromyoma 5 cm. in diameter. She was seen at the follow-up clinic 6 weeks postoperatively and complained of lower abdominal pain but no bleeding. With consultation from the Medicine Department it was felt that the patient's general condition would not permit further surgery.

CASE 11. A. M. G., 26 year old colored female, seen in the emergency room on Sept. 29, 1942, in a state of shock. The only history that could be obtained was that she had been getting along very well until the morning of admission when she had had a sudden massive hemorrhage per vaginum. On examination the patient was confused, restless, pale, and perspiring freely. Pulse was counted at 150. The hemoglobin level was so low that it could not be determined. She was given immediate shock therapy and her blood pressure rose to 100/60. On pelvic examination she was found to have a tumor the size of an orange with a ragged surface filling the vaginal vault and suspended from within the cervical canal by a pedicle approximately 1 cm. in thickness. She was given supportive therapy and daily blood transfusions for five days and the morning of the sixth hospital day the pedunculated submucous fibromyoma was severed from its pedicle and delivered. The pedicle was cauterized and no bleeding followed. She was given only supportive measures postoperatively and her hospital course was uncomplicated. Pathology reported a detached fibromyoma 9 by 6.5 cm. with ulceration of the surface. She was not seen again following hospitalization.

CASE 12. M. J., 38 year old colored female, admitted to the hospital Aug. 19, 1941, with a history of having started bleeding one month previously at the time of her regular menses. The bleeding was profuse at first but lessened so that she was only spotting on admission. She related having had a similar episode of menorrhagia one year previously but her periods had been at regular intervals with some increased flow until her present bleeding. She had had four pregnancies during 20 years of marriage resulting in three full term living children, the youngest 10 years of age, and one abortion at three months' gestation which followed her last full term delivery. On examination she was an undernourished anemic Negress with a hemoglobin value of 5.5 Gm. A blowing Grade 2 systolic murmur was audible at the apex. The abdomen was distended by a hard nontender nodular mass arising from the pelvis and extending to the umbilicus. The pelvic examination revealed a tumor approximately 3 cm. in diameter occupying the upper vaginal vault with an attached pedicle running up into the cervical canal. Whole blood transfusions were begun and she was taken to the operating room where the tumor was snared from the pedicle which retracted and could not be identified. The uterine cavity was packed to control bleeding but upon removal 24 hours postoperatively slight bleeding ensued and she had serosanguineous discharge for three days. The pathological examination revealed an amputated fibromyoma 3 by 2

cm. partially necrobiotic; necrosis of the atrophic covering epithelium. This patient was seen eight weeks postoperatively with no complaints but was advised to have an hysterectomy which she refused.

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GIANT PULMONARY CYST, SIMULATING SPONTANEOUS PNEUMOTHORAX

R. F. Corpe, M.D.*
J. L. Alexander, M.D.**
I. Stergus, M.D.***
A. Cuadrado, M.D. ****
Augusta

Since 1925, when Koontz first brought to general attention congenital cystic disease of the lungs, the condition has come to be widely recognized, and is no longer considered a medical rarity. While congenital malformations are usually brought to light during early childhood, it is known that congenital cysts may lie dormant until well into adult life, until attention is drawn to them by infection, rupture, or other complications.

The diagnosis of uncomplicated cystic disease is usually made by accident, the condition being discovered by a routine x-ray taken for some other reason. When complications arise, the symptoms are those of the complicating factor, depending on the presence of infection or hemorrhage, and the size and location of the cysts. The cysts are usually multiple, but may be single. Slight predilection is shown for the upper pulmonary segments. In order of frequency, the symptoms are cough, expectoration, hemoptysis, and pain. These are nonspecific symptoms, pointing only to pulmonary pathology. Rarely, because of size, or extensiveness of involvement, symptoms brought about by the cysts per se are present. Roentgenography is the sole method of establishing definitely the diagnosis. The typical picture is that of single or multiple annular rarefactions, involving one or both pulmonary fields, usually with thin walls and little or no surrounding pulmonary reaction. The presence of infection, of course, changes the picture, giving rise to fluid levels and perifocal infiltrations. This change, however, is rarely as extensive as that seen in pulmonary abscess or cavitary tuberculosis. On occasion, when a solitary cyst reaches huge proportions, so that it fills the entire hemithorax, the differentiation between pulmonary cyst and total pneumothorax becomes difficult, and at times may be made only by exploratory thoracotomy.

Spontaneous pneumothorax was, for many years, considered to

*Chief of Surgery, Battey State Hospital. Member of the U. S. Public Health Service on active duty. The opinions in this paper are his own and do not necessarily reflect the opinions of the U. S. Public Health Service.

**Resident in Thoracic Surgery, Battey State Hospital; now Resident in Thoracic Surgery, University Hospital, Augusta, Georgia.

***Department of Pathology, Battey State Hospital.

****Member of the Medical Staff, Battey State Hospital.

be prima-facie evidence of pulmonary tuberculosis. It is now known that tuberculosis is rarely a cause of spontaneous pneumothorax, and that the most common cause is the rupture of an emphysematous bleb. The symptoms of spontaneous pneumothorax depend on two factors: the extent of the initial pneumothorax, and the presence or absence of factors leading to the development of tension pneumothorax. Ordinarily, the pneumothorax is small, the pleural defect rapidly closes, and the intrapleural air is absorbed without intervention. In this case, the only symptoms may be chest pain, commonly radiating down the homolateral arm, and varying degrees of dyspnea. If, however, the pleural defect forms a ball-valve mechanism, or if the bronchopleural fistula is so large as to make prompt closure impossible, a tension pneumothorax develops. Dyspnea becomes severe, and cyanosis may develop. The symptoms do not tend to abate, and the hemithorax must be deflated. The onset is usually abrupt and dramatic, and the symptoms are terrifying to the patient. If left untreated, death from anoxia is a not uncommon sequel. Gradations of symptomatology, depending entirely on the rapidity and duration of the air leak, exist in cases of spontaneous pneumothorax, between mild and inconsequential to severe and fatal.

Recently, at Battey State Hospital, we have had the opportunity to see a case of giant pulmonary cyst which simulated spontaneous, total pneumothorax. Interesting diagnostic problems arose in this case, which were finally solved only by exploratory thoracotomy.

Case History

This 36 year old colored female, S. G., a housewife and farm worker, was admitted to Battey State Hospital on Feb. 5, 1951, with the complaints of cough and dyspnea since December 1950. A history of her present illness dated back to August 1950, at which time her last child was born, and from that date she felt weak, although had no other symptoms. In October 1950, she started to have a cough. The cough was dry and nonproductive, at that time, and was associated with some pleuritic type of pain in the right lower chest. There was no appreciable fever. She was treated with penicillin and cough medicine for a period of two or three weeks. The cough was somewhat relieved. Some time before Christmas of 1950, while the patient was in bed, she felt as if something burst inside her right chest and she was seized with acute shortness of breath. With that episode, a doctor was called and an x-ray of the chest subsequently indicated the total absence of lung shadow in the right chest. Her dyspnea improved somewhat, but she was still unable to sleep flat in bed. The past history was noncontributory. The review by systems was noncontributory. The positive findings on physical examination were: no expansion of the right chest, vocal fremitus and breath sounds were totally absent in the right chest and the entire right chest was hyperresonant. By percussion, on the time of admission, the heart was in normal position. Fluoroscopy, on the original work-up, revealed the right diaphragm to move

only slightly. Movements of the left diaphragm were normal. A complete blood count was done. This was within normal limits on Feb. 6, 1951, and a blood Kahn was negative. Urine analysis was negative. Specimen of feces was negative for intestinal parasites. The admission radiographic report on

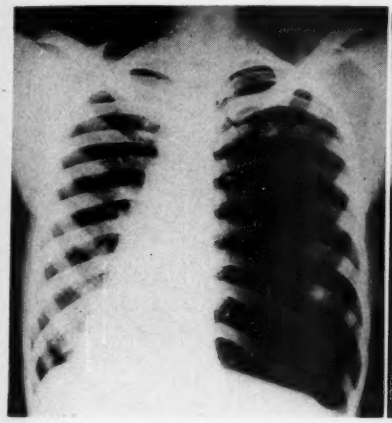

Fig. 1. The right lung is completely collapsed and the right chest is filled with air shadows.

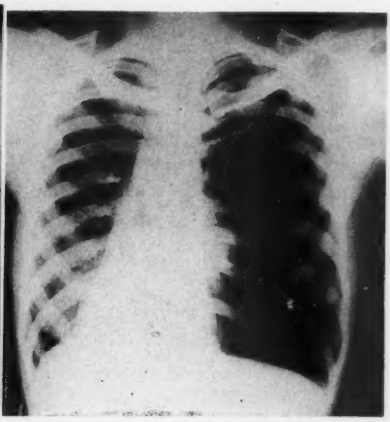

Fig. 2. On reviewing this x-ray, after knowing the operative findings, one can definitely make out the edge of the cyst just medial to the medial edge of the scapula. The significance of this line was not fully appreciated preoperatively.

February 6 was as follows: "The right lung (fig. 1) is completely collapsed and the right chest is filled with air shadows. The right costophrenic angle is obliterated due to adhesions. The left lung shows no significant abnormal shadow. *Classification:* Undetermined at the present time. This is apparently a spontaneous pneumothorax possibly due to tuberculosis. Comparison with application film shows no significant change and there has been no evidence of any re-expansion of the right lung." (CBS)

This case history was presented at General Staff Conference by one of us (A.C.) who believed this represented a case of giant lung cyst. It was the opinion of the majority of the staff members that this represented a spontaneous pneumothorax. A diagnostic work-up followed. In the diagnostic work-up of this patient, right thoracentesis on February 14 revealed an initial pressure of —1 —3. It changed to —7 +7 on deep breathing. Three thousand cc. of air was withdrawn without discomfort, leaving a final pressure of —3 —5, changing to —5 +5 on deep breathing. An attempt to establish an intrapleural pneumothorax was not satisfactory. Fluoroscopy following thoracentesis on this date did not reveal any change. On February 16, right thoracentesis of 3,000 cc. of air was again carried out. The initial pressure was —2 —5; the final pressure was —2 —5. Following this, fluoroscopy revealed a less marked mediastinal shift and some slight re-expansion of the lower lobe. This was confirmed by x-ray. On February 21, thoracentesis was again carried out with the removal of 4,500 cc. of air. Initial pressure was —4 —5 and the final pressure was —6 —6. Four cc. of methylene blue was instilled. This

methylene blue was never recovered nor sighted in any sputum specimen. Fluoroscopy revealed both lower and middle lobes to be re-expanding. X-ray confirmed this (fig. 3). This re-expansion at this time was no more than 15 per cent.

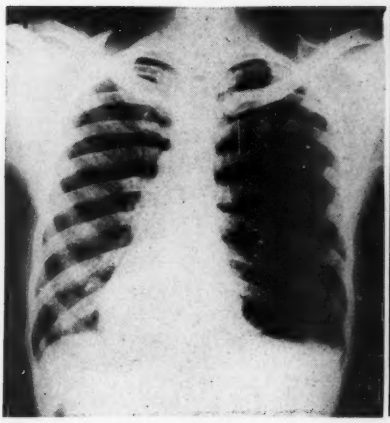

Fig. 3. Note both lower and middle lobes to be partially re-expanded.

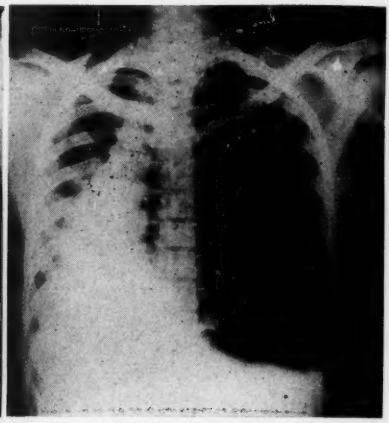

Fig. 4. Right lung again completely collapsed.

On February 23, thoracentesis of 3,500 cc. of air was again carried out with a final pressure of —3 —6. Fluoroscopy following this revealed the lung to be nearly 50 per cent re-expanded. On February 27, fluoroscopy before

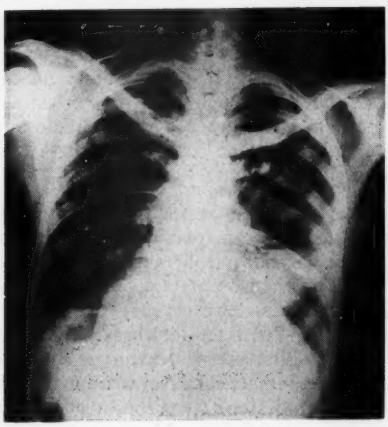

Fig. 5. Immediate postoperative re-expansion of right lung.

thoracentesis revealed the right chest empty and the lung completely collapsed as before. The mediastinum was shifted toward the left. There was a small amount of fluid at the base and 350 cc. of serosanguineous fluid was aspirated. No air was withdrawn. On February 28, fluoroscopy revealed the right lung

entirely collapsed with mediastinal shift to the left. There was only an insignificant amount of fluid at the base. Thoracentesis of 1,500 cc. of air was carried out and, again, fluoroscopy following this revealed the lung to be expanded approximately 30 per cent. Thoracentesis of 1,000 cc. of air was again

Fig. 6. Photograph of the open cyst in situ. The retractor is displacing the upper lobe and just to the left of the retractor can be seen the point of air leak into the cyst. The thin trabeculated nature of the cyst wall is well demonstrated in this photograph.

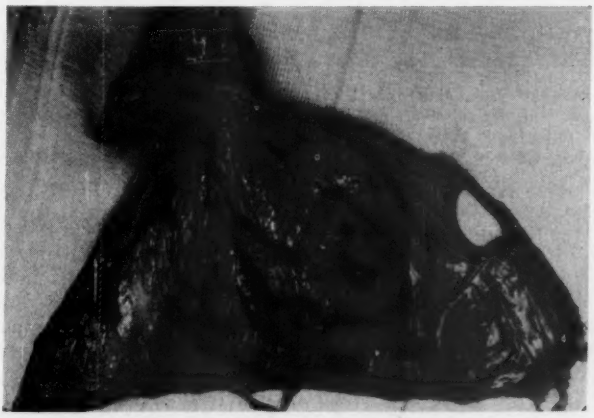

Fig. 7. Photograph of the cyst after removal. The cyst is seen arising from the lateral segment of the middle lobe and the inflated middle segment is seen at the top of the picture. The point of air leak into the cyst is well demonstrated in the mid portion of the base of the cyst. Note the extremely large dilated vessels coursing through the walls of the cyst.

carried out on March 2, without re-expansion of the lung. An expiration film on March 6 again reveals, roentgenologically, the complete collapse of the right lung with evidence of trapped air (fig. 4).

The diagnostic work up to this date, we felt, pointed more to a spontaneous pneumothorax, but the possibility of intracystic air withdrawal had not been ruled out. It was our feeling that exploratory thoracotomy was in order. An exploratory thoracotomy was then carried out on March 29. At the time of exploratory thoracotomy, there was found to be a huge cyst occupying the entire right hemithorax and collapsing the entire right lung, which was lying anteromedially.

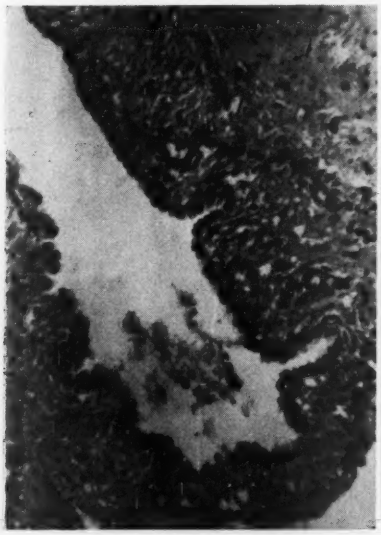

Fig. 8. Low power photomicrograph of the cyst showing the columnar cell lining and underlying moderately scattered muscle bundles.

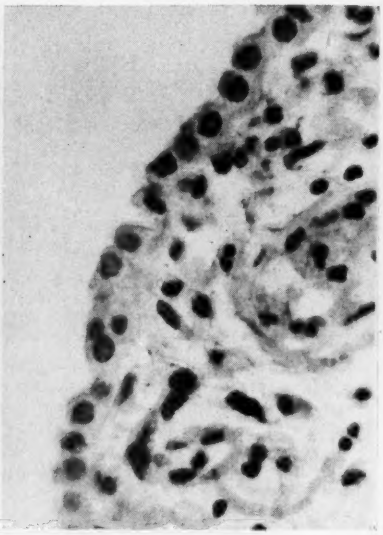

Fig. 9. High power photomicrograph of the ciliated columnar epithelial lining.

The cyst was densely adherent to the lateral chest wall below the level of the sixth interspace, anteriorly, and also to the diaphragm and to the lateral surface of the right lower lobe. The cyst was found to arise from the right middle lobe. There was no evidence of any palpable or visible pathological process within any of the three lobes other than the cyst of the middle lobe. The cyst wall was shiny and tissue paper thin, especially over the upper portion of the cyst. All of the cyst over the lateral surface of the lower lobe and diaphragm and lower chest wall was considerably thickened with a few fairly good sized vessels coursing through it. After the cyst had been opened, one could see three definite points of air leakage into the cyst, all of which came from the lateral segment of the right middle lobe. A right middle lobectomy and decortication of the lower lobe and diaphragm was performed. The postoperative course of the patient was benign. The lung re-expanded nicely (fig. 5). The patient was discharged from the sanatorium on March 21, 1951.

Pathology: Specimen of a right middle lobe which is considerably collapsed and measures 10 by 4.3 by 1.5 cm. weighing 85 Gm. The external surface is for the most part smooth and of dark reddish brown to lavender gray color

showing a few better serated pinkish lavender areas. On the lateral surface a previously opened thin vascular pinkish red sac-like structure is attached 14 by 15 by 0.3 cm. which shows more extensive fibrosis at the focus of attachment to the middle lobe. The medial and lateral branches of the middle lobe bronchus are separately tied off. No direct communication from these branches into the cyst can be shown on injecting methylene blue or dissection. Injected air, however, is seen to escape in bubbles from two rather thinned areas of the cyst wall, attached to the underlying pulmonary tissue. An occasional bubble of air is observed in the lumen of the lateral bronchial branch. There is a small shallow excavation in the most central portion of the attached thickened cyst wall. Several sections of parietal thickened pleura are received with the specimen.

Microscopics: Serial sections through the cyst wall reveal in most areas a markedly compressed unidentifiable lining especially in those where the wall is thickened. In several foci, however, a definite epithelial lining can be made out varying from moderate high cuboidal to columnar in type. Even a few rather poorly preserved and clumped ciliae can be made out in the more delicate portions of the wall. The latter is made up of a dense in part hyalinized connective tissue and smooth muscle showing foci of nonspecifically arranged lymphocytic and plasma cell infiltration with moderate fibroblastic activity and slightly dilated capillaries. In some areas quite dense hemosiderin deposits are observed, evidencing previous hemorrhage. No histopathological pattern of tuberculosis is seen in any of the sections. Sections through the middle lobe adjacent to the cyst wall reveal the alveoli to be of about normal size. The flat cuboidal epithelium shows no noteworthy changes. The bronchi are lined by pseudo-stratified well preserved ciliated columnar epithelium. There is a scant lymphocytic and plasma cell interstitial infiltrate with an occasional fibroblast. A few macrophages are present within the bronchial lumina.

Diagnosis: The findings are consistent with a giant pulmonary cyst, right middle lobe, bronchogenic. (IS)

A case history of giant pulmonary cyst, closely resembling a spontaneous pneumothorax, including the diagnostic steps, and roentgenological procedures has been presented. A brief résumé of the major clinical factors of congenital pulmonary cystic disease, and of spontaneous pneumothorax is given.

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ADRENAL VIRILISM IN A THREE YEAR OLD GIRL

ROBERT B. GREENBLATT, M.D.*
RALPH HILL CHANEY, M.D.**
SARAH L. CLARK, M.S.***
Augusta

SOME 76 cases of adrenal tumor in children up to 12 years of age have been reported in the literature.[1-17] Forty-six fell into the category of the adrenogenital or corticosexual syndrome with evidences of excess androgen production. Twenty-six were of the Cushing's syndrome type with manifestations of hypercorticoidism such as obesity, diabetic sugar curve, weakness, hypertension and plethora. One case was that of a feminizing adrenal tumor causing gynecomastia in a boy of 5 years of age.[7] Three of the cases were diagnosed as aberrant adrenal rest tumors or hypernephromas of the ovary.[15-17] It is noteworthy that the preponderance of the adrenal tumors occurred in females, *i.e.*, 58 cases.

Some of the salient features of adrenal virilism in female children are increased bone age and height, increased muscular development and strength, acne or seborrheic dermatitis, malelike larynx and voice, hypertrichosis, enlarged clitoris and hypertrophy of the labia. As a rule, these patients excrete an excess of 17-ketosteroids in the urine[18] and a high excretion of urinary pregnandiol is not uncommon.[17-22]

Perirenal air insufflation according to the technic of Cahill[23] and intravenous pyelography are very useful aids in diagnosing the size and location of adrenal tumors. The Allen color test for dehydroisandrosterone[14] in the urine is a rapid laboratory procedure which will help to distinguish adrenal tumor from congenital adrenal hyperplasia (female pseudohermaphroditism). High quantities of dehydroisoandrosterone are excreted by patients with masculinizing adrenal tumors. As Wilkins has pointed out,[24] congenital adrenal hyperplasia may be distinguished from adrenal tumor by the finding of embryonic defects such as a urogenital sinus in female pseudohermaphroditism. Exploratory surgery is generally necessary to distinguish between virilism due to tumor and that caused by postnatal adrenal hyperplasia. Alterations of serum cholesterol and/or albuminuria are usually found in patients with adrenal virilism.

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*Professor of Endocrinology.
**Professor of Clinical Surgery.
***Research Assistant, Endocrinology.
From the Departments of Endocrinology and Surgery, Medical College of Georgia.

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The purpose of this paper is to record a case of postnatal virilism in a 3 year old Negro girl due to an adrenal tumor.

Case Report

W. D., a colored female, aged 3½ years, was referred to the senior author by Dr. Paul Bradley of Dalton, Georgia. Physical examination on Jan. 12, 1951, revealed a rather tall, thin, poorly nourished child with a protuberant abdomen (fig. 1). Her weight was 36 pounds and her height 110 cm. The

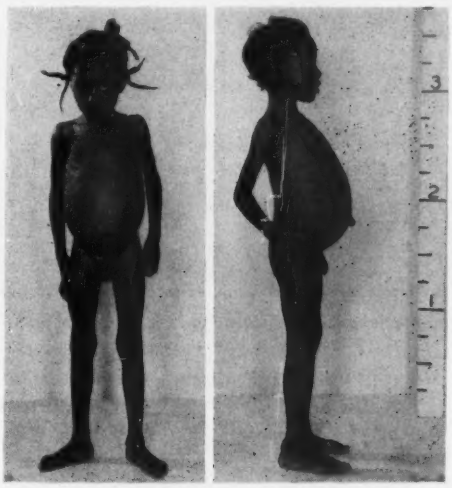

Fig. 1. Note protuberant abdomen in a girl aged 3½ years with large adrenal tumor. Note pubic hair.

temperature was 99, pulse 142, respiration 20. The blood pressure was 128/84 mm. Hg. Examination of the genitalia revealed an infantile vaginal introitus allowing passage of a catheter into the vaginal canal for a distance of 5 cm. The clitoris was markedly hypertrophied, measuring 4 cm. in length. The vaginal smear was castrate. The vulvae were well developed. An abundance of pubic hair was present (fig. 2). There was a slight growth of axillary hair but no facial hair. A large tumor mass was palpable in the left upper quadrant with a notch in the center extending towards the pubic symphysis. A second tumor mass was present in the mid-abdomen, extending in an oblique diameter from just above the umbilicus downward toward the right flank (fig. 3).

From the history given by the child's parents it was learned that pubic hair had been present since early infancy. Weight loss and anorexia had begun six months prior to her examination here. Shortly thereafter she began to complain of postprandial abdominal pain and to vomit one meal daily. The tumor masses had gradually increased in size over the six month period. The child's four siblings are said to be normal; her mother and aunt are slightly hirsute.

Laboratory Findings: Red blood count 3,810,000. White blood count 12,-

700. Hemoglobin 9.2 Gm. Differential: neutrophils 65 per cent; lymphocytes 34 per cent; monocytes 1 per cent; basophils 1 per cent. No sickling at 48 hours. Circulating eosinophil count — 19 per cu. mm. Blood Kahn test was negative. Stool examination was negative for ova and parasites. Urinalysis

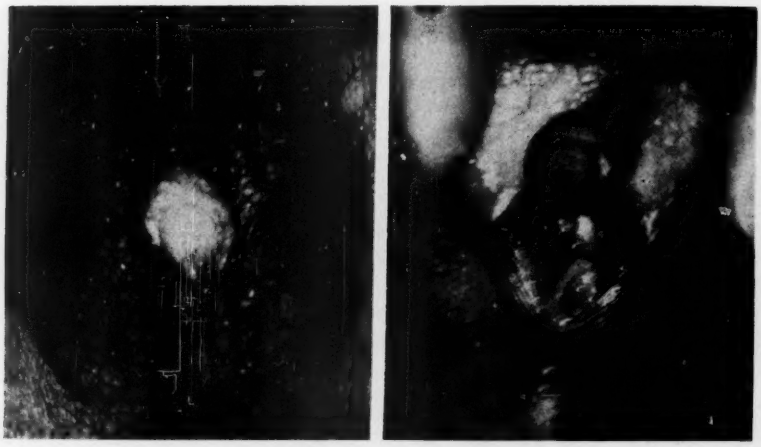

Fig. 2. Note enlarged clitoris and normal vaginal introitus and the abundance of pubic hair.

showed a trace of albumin; otherwise negative. The Allen test for dehydroisoandrosterone in urine was strongly positive with 3 drops of urine. The 17-ketosteroid excretion[25,26] and pregnandiol excretion[17] were markedly elevated. The corticosteroid output[28] was within normal range.

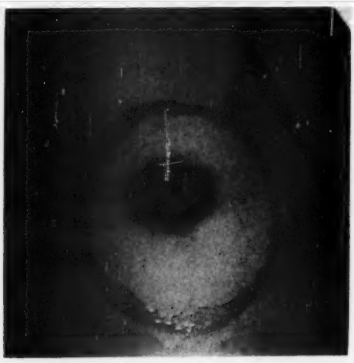

Fig. 3. Rough outline of two abdominal masses.

X-Ray Findings: X-rays showed her bone age to be ten plus years (fig. 4). AP view of the abdomen revealed a "large mass in the left upper quadrant which extends downward to the left iliac crest, some calcification in the central portion of this mass. Another mass approximately 10 cm. in diameter in

central portion of the abdomen in the region of the umbilicus (fig. 5). PA and lateral views of the chest demonstrated no definite evidence of metastases."

Exploratory surgery was deemed advisable. The patient was prepared preoperatively with Gantrisen (0.25 Gm. every 4 hours) for two days, and on the day preceding surgery, ACTH (Armour) was administered in doses of 10 mg. every six hours. An infusion of whole blood (1 pint) was given slowly the night before surgery.

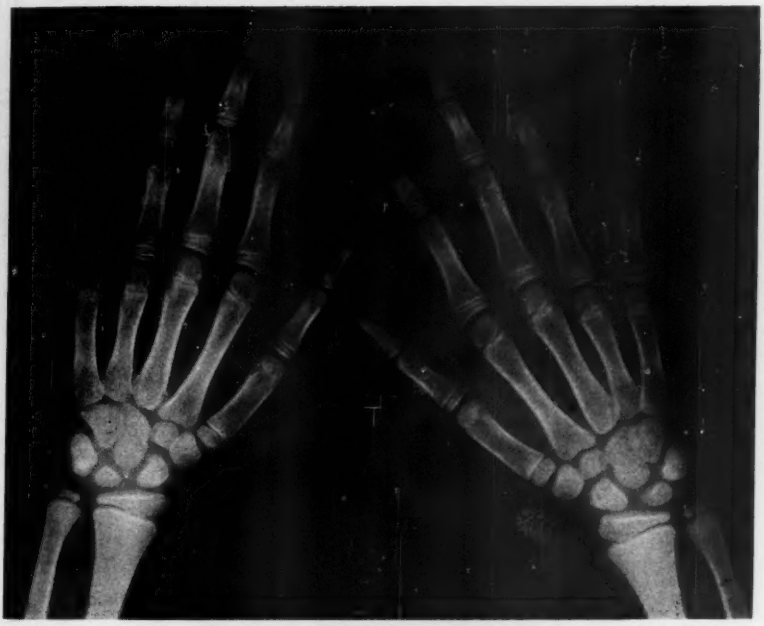

Fig. 4. Roentgenogram of wrist. Note advanced bone age (about ten years) of the child shown in Fig. 1.

On Jan. 16, 1951, the peritoneal cavity was entered through a left paramedian incision some 17 cm. in length. Immediately upon entering the peritoneal cavity a large tumor mass measuring approximately 8 by 10 by 12 cm. was encountered. (This was first interpreted as a tumor of the right adrenal but turned out to be the lobulated portion of the massive left adrenal tumor.) The left hypochondrium was next explored and a tremendous retroperitoneal tumor was encountered which displaced the splenic flexure medially. The spleen was small and pushed upwards. The central tumor mass was removed. During the process of removal, this tumor was ruptured. It was felt inadvisable to attempt to remove the main tumor at this time and the abdomen was closed.

During surgery the patient was given one pint of blood containing 10 cc. of aqueous adrenal cortical extract (Upohn) and one liter of 5 per cent glucose

The ACTH was supplied by Armour Laboratories through the courtesy of Dr. John R. Mote.

in distilled water. Postoperative treatment included 2 cc. of lipo-adrenal cortex (Upjohn) stat. and 1 cc. daily for eight days following the operation. She also received penicillin and Gantrisen, routine postoperative fluids and liquids, and a soft and regular diet. During the first eight postoperative days

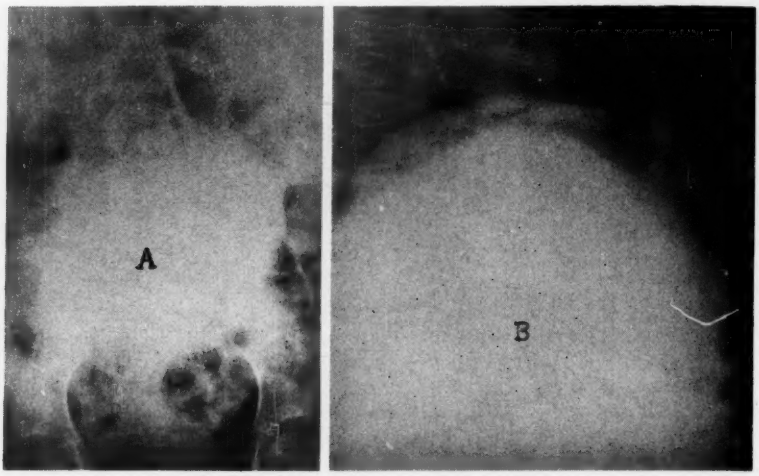

Fig. 5. Roentgenograms of abdomen—note dense tumor masses.

the blood pressure varied from 110/70 to 140/95, becoming 102/57 by the twelfth postoperative day. The pulse during this time ranged from 96 to 130. The postoperative course was smooth and uneventful.

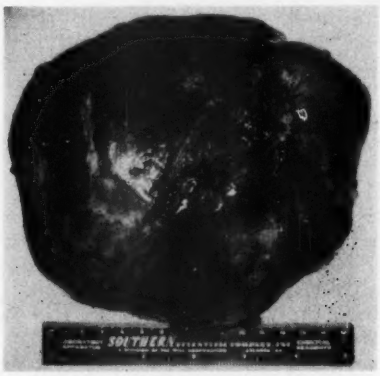

Fig. 6. Large adrenal tumor.

The pathology report by Dr. Edgar R. Pund on the tumor excised on Jan. 16, 1951, was as follows: "A disrupted tumor of adrenal cortical origin consisting of a saccular fibrous capsule which has been previously opened, size

The Lipo-Adrenal Cortex used in this study was supplied through the courtesy of Dr. H. F. Hailman, Upjohn Company, Kalamazoo, Michigan.

estimated at 8 cm. in diameter, to which is adherent at one aspect a plaque-like mass of necrotic tissue some 4 cm. in diameter. The neoplasm proper is composed of numerous soft friable fragments, the overall dimensions are 9 cm. in diameter, and composed of mature type of adrenal cortical cells. Scattered throughout are numerous giant swollen cells with degenerated forms rather than true tumor giant cells. The tumor therefore appears to be an adenoma of the suprarenal but, because of disruption, it cannot be determined if there was complete removal. Extensive areas of necrosis throughout the neoplasm."

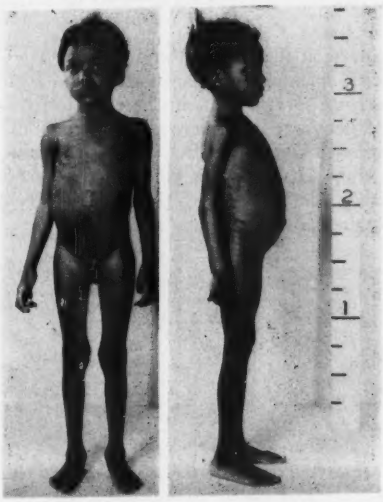

Fig. 7. Excellent recovery after both operations.

On January 22 (six days postoperatively) an intravenous pyelogram was done and revealed a normal right ureter and kidney with no evidence of renal function on the left. On January 29, a P.S.P. excretion test was performed and 60 per cent elimination of the dye was obtained in two hours. A complete blood count on January 31 was as follows: Red blood count 4,100,000; white blood count 14,200; hemoglobin 9.8 Gm.; differential-neutrophils 76 per cent, lymphocytes 22 per cent, monocytes 2 per cent.

The patient recovered progressively and was brought to surgery again on Feb. 1, 1951. She received 15 mg. of ACTH every six hours and one pint of whole blood on the day prior to surgery. Surgery was performed by a trans-peritoneal approach through a left oblique subcostal incision. A large, firm retroperitoneal tumor was exposed which measured roughly 18 by 14 by 12 cm. and displaced the splenic flexure of the colon medially and anteriorly. The tail of the pancreas was noted to be in close proximity to the tumor. As the left kidney was involved in the tumor mass, left nephrectomy was accomplished along with removal of the tumor (fig. 6). On exploration of the pelvis a normal uterus, fallopian tubes and ovaries were demonstrated.

During the surgical procedure the patient received four pints of whole blood and 500 cc. of 5 per cent glucose and her condition was satisfactory at the conclusion of the operation. Her blood pressure was never over 120/76

or under 95/55 postoperatively; the pulse varied between 118 and 90. ACTH was administered postoperatively for eight days, *i.e.*, 15 mg. every 6 hours for four days, 15 mg. on the fifth and sixth days, 10 mg. on the seventh day, and 5 mg. on the eighth day. She received 1 cc. of lipo-adrenal cortex daily for five days beginning on February 3. Her supportive postoperative therapy was similar to that given after the first operation with the exception that Chloromycetin, 500 mg. every eight hours was added for five postoperative days. The child made an uneventful recovery and was dismissed from the University Hospital on Feb. 24, 1951, with a blood pressure of 105/75 and weight of 34 pounds (fig. 7).

The pathology report on the second tumor removed was as follows: "Adenoma of the suprarenal forming an encapsulated mass 20 by 15 cm. and weighing 1260 Gm. There are several rents in the capsule from which are extruded several fragments of neoplasm. Numerous large areas of necrosis throughout the tumor. The adenoma compresses but does not invade the attached kidney and attenuates the upper half of the kidney." Some of the cells contained lipoid vacuoles which is compatible with the high urinary 17-ketosteroid excretion (fig. 8). Ponceau-fuchsin stain was not done.

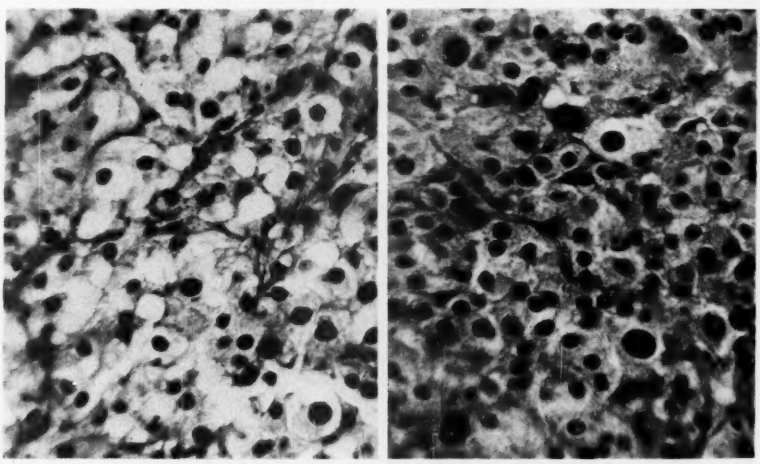

Fig. 8. Two histopathologic sections of adrenal cortical tumor.

An analysis of the left adrenal tumor tissue revealed a total 17-ketosteroid content of 45.2 mg. The patient's urinary 17-ketosteroid excretion had returned to normal by Feb. 8, 1951 (2.8 mg. per 24 hours), and the Allen color test for dehydroisoandrosterone was negative on this date, suggesting that all of the adrenal tumor tissue had been removed. It is interesting to note that the circulating eosinophil count rose from 19 per cu. mm. preoperatively to 115 per cu. mm. on February 3 after the second operation, and to 481 per cu. mm. on February 23, indicating a relative decrease in adrenal cortical reserve.

At this writing, the child has returned for further observation. She did well for three months, having gained in weight. Some regression in size of the

TABLE 1

Urinary Hormonal Assays
(expressed in mg. per 24 hours)

Date	17-Ketosteroids	Pregnanediol	Allen Test	Corticosteroids	Creatinine	Creatine
1-14-51	228.7	19.6	Pos.	0.65	202	39
1-15-51	102.3	18.0	....	0.27	148	50
1-16-51	Excision of central tumor					
1-21-51	324.0	18.4	....	0.72	270	14
1-22-51	199.6	23.5	....	0.13	107	78
1-23-51	257.0	31.1	....	0.07	232	0
1-24-51	132.2	42.6	....	0.10	260	220
1-25-51	115.0	...	....	0.06	...	...
1-26-51	130.0	...	....	0	226	185
1-27-51	318.6	...	....	0.16	480	180
1-28-51	289.8	...	....	0.08	240	82
1-29-51	222.7	...	....	0.18	224	26
2-1-51	Excision of left adrenal tumor					
2- 8-51	2.8	...	Neg.	0.23	207	0
2- 9-51	1.4	...	Neg.	0.08	89	0
5-15-51	194.4	...	....			
5-16-51	248.0	...	....	0.32	282	141
5-21-51	709.0	...	Pos.	0.23	328	296
6-18-51	521.0	...	....	Recurrence with metastases		

clitoris and some loss of pubic hair were noted. From May 1, 1951, however, a gradual change from her feeling of well being took place and she began to complain of loss of appetite, nausea and abdominal pains. Examination failed to reveal any recurrence of tumor masses but hormonal assays are strongly indicative of recurrence. The Allen test for dehydroisoandrosterone has again become strongly positive; the 17-ketosteroid excretion has increased to 248 mg. per 24 hours. The eosinophil count has dropped to 115 per cu. mm. The patient has been readmitted for deep x-ray therapy. By early June pulmonary metastates could be demonstrated. Local recurrence has taken place. Urinary 17-Ketosteroids have risen to over 500 mg. per 24 hours.

Summary and Conclusions

A case of adrenal virilism in a 3 year old Negro girl is presented. The salient features of her syndrome were advanced bone age, enlarged clitoris and hypertrichosis. Urinary hormonal studies revealed markedly increased androgen and pregnanediol excretion and normal urinary corticosteroid values. A large lobulated abdominal tumor mass was palpable.

Removal of the central adrenal mass and the left adrenal tumor was accomplished in two stages. ACTH and Lipo-Adrenal Cortex were administered pre and postoperatively as prophylaxis against adrenal crisis. The patient made an excellent recovery following

both surgical procedures and enjoyed good health for a period of three months. During this time there was a gain in weight of eight pounds and there was some regression in the size of the clitoris and in the amount of pubic hair. Unfortunately, in the past few weeks there has been a return of nausea, loss of appetite and abdominal pains.

After removal of the adrenal tumor the urinary 17-ketosteroids, which averaged about 200 mg. per 24 hours before operation, returned to normal (about 2 mg. per 24 hours) and the Allen test for dehydroisoandrosterone became negative. With the return of the patient's complaints the Allen test became strongly positive and the 17-ketosteroid excretion returned to the preoperative levels. This is indicative of a recurrence of the tumor and the patient has been rehospitalized for deep x-radiation therapy.

This case illustrates the value of urinary hormonal assays in differentiating between virilism due to adrenal tumor, adrenal hyperplasia and Cushing's syndrome. The importance of hormonal assays in the early detection of postoperative recurrence is illustrated.

The authors wish to acknowledge with thanks the cooperation of Dr. Paul Bradley of Dalton, Georgia, who referred the case of adrenal virilism to them.

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FATAL PULMONARY EMBOLISM

With Special Reference to Pelvic Thrombosis as an Origin

JOHN P. WILSON, M.D.*
Augusta

DESPITE the great amount of work which has been done on the problem of thrombo-embolism and the numerous articles written on the subject in recent years, we find ourselves today still unable in many ways to deal effectively with this disease entity.

We are at present in a period of evaluation of the newer methods of treatment of thrombo-embolism. Sufficient time has elapsed and enough clinical experience has been gained for a critical and comprehensive appraisal of these therapeutic measures. We find that many of the early optimistic reports in the use of anticoagulants and venous ligation have been superseded by less encouraging evaluation and the indications for their use, particularly venous ligation, presented with more caution. Dehlinger and Riemenschneider,[22] Ravdin and Kirby,[63] and Ochsner et al[60] have, with others, noted the failure to significantly reduce the mortality due to pulmonary embolism with the use of current therapeutic measures.

This evaluation has not discredited the use of either method but rather has defined its indications and limitations. Both have been proved to be valuable adjuncts in the treatment of thrombo-embolism and are the most specific and promising, to date, of the myriad of therapeutic measures and technics which have been advocated, including exercise, positioning of patients, drugs, etc. Both do, however, have their shortcomings and dangers.[6,21,29,63] Venous interruption, whose advocates have employed procedures ranging in extensiveness from superficial femoral to vena caval ligation, has, in particular, been shown to have its hazards, undesirable sequelae and therapeutic ineffectiveness.[1,2,4,29,50,64,68,69] Although the effectiveness and safety of anticoagulant therapy, both with heparin and dicumarol, has increased with experience in use, it is not without its dangers and shortcomings in therapeutics.[28,74]

The significance of various predisposing factors such as age, stasis, obesity,[37,65,67] seasonal variation,[3,18,59] regional variation,[4,59] sex,[18,40,45,46,73] trauma,[34,47] and operations, particularly of the pelvis,[17,20,36,44,52,59,73] has been enumerated.

It is, however, the nature of the embolus-producing thrombosis, upon which the preventive treatment of pulmonary embolus is based,

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From the Department of Surgery, Medical College of Georgia.
*Assistant Resident, Surgery.

with which this paper is chiefly concerned. The two principal factors concerned are the amount of inflammation and the position of the thrombus.

Probably the greatest difficulty encountered in the treatment and prevention of thrombo-embolism, particularly of the massive type, has been its, for the most part, asymptomatic character, this being due to the minimal amount of inflammation and, consequently, minimal fixation. By its very nature the "silent," "bland" thrombus or "phlebothrombosis" is the most likely to give rise to a massive embolus. The lack of inflammation,[9,70,75] whether this type of thrombosis is a separate entity from thrombophlebitis or the first stage of a process which will later become inflammatory, makes the early diagnosis difficult and the thrombus lethal. However, although the massive type embolus is usually of a bland nature, the presence of inflammation does not necessarily exclude the possibility of an incipient pulmonary embolus.[7,25,29,57] Often there is no warning prior to the fatal embolus,[23,27,34,36,72] this in spite of increased awareness of the condition.[73]

It is chiefly this asymptomatic character which has led to the use of prophylactic ligation of superficial veins, although this process in itself provides one of the factors (*i.e.,* damage to the intima) in phlebothrombosis formation.[64] It is also this silent nature of massive thrombosis which has led to the search for a clinical test to recognize the impending embolus.[60,66]

It should be noted here that there is evidence[15,16,17,51,58,75] that not infrequently a pelvic thrombophlebitis through the process of suppuration and liquefaction gives rise to pulmonary embolus, sometimes fatal.

It has only been in the past 20 years or so that the site of origin of pulmonary emboli has been extensively studied and it has been during that period that the realization of the frequency with which emboli arise from the veins of the leg has occurred.

Since the work of Virchow in 1856 and later Aschoff, the general principles of thrombo-embolism have been recognized. Although the relationship of leg symptoms and thrombosis had been noted, it was Homans[38] in 1934 who first presented the picture of a bland thrombus, originating in the small veins of the leg giving rise to pulmonary embolus, as a clinical entity. The work of Roessle and Newmann in 1937 and 1938 and their finding of an extremely high incidence of thrombi in calf and foot veins stimulated the concept of pulmonary emboli arising from small veins of the legs and foot. Frykholm[30] in 1940 contributed to the knowledge of the location of thrombi in the lower extremities, and during this period there was

generally, as reflected in the literature, an emphasis on the importance and frequency of the veins of the legs as a source of pulmonary emboli.

The concept of a long bland propagating thrombus beginning in the veins of the lower extremity as the usual source of pulmonary embolus, particularly a massive one, has been well established.[10,11,38,39,41,42,55,56,57]

In practical clinical application of therapeutic measures it is not quite so simple, for although there is no great amount of inflammation, the proximal extension and fixation, even of thrombi arising deep in leg veins, is sufficient to prevent surgical correction by the usual ligation (superficial femoral).[6,19,22,39,43] The frequency with which this occurred led to the advocation of higher and more extensive ligations, the results of which have often not been satisfactory.

While it is quite true that most massive pulmonary emboli arise from thrombi in the veins of the lower extremity, some arise from other sources, in particular the veins of the pelvis. This fact has perhaps become somewhat obscured by the emphasis of the extremity veins as a source. Although the source is possibly not particularly pertinent in anticoagulant therapy, a consideration of the possible origin of an embolus is essential to diagnosis and institution of therapeutic measures both as to when and what type.

Pulmonary emboli have been reported as arising from a number of locations other than the lower extremities. In particular, mural cardiac thromboses have been noted to give rise to pulmonary emboli. Some investigators report the splenic vein as a not infrequent source. Bailey[5] has reported the ovarian veins as a rare source. However, massive fatal pulmonary emboli rarely arise other than from the extremity or pelvic veins. It is the frequency with which the latter give rise to pulmonary emboli that is to be considered here.

There is considerable difference of opinion in the literature as to how often the pelvic veins give rise to pulmonary emboli. This is due in large part to the difficulty in determining the source of an embolus. Clinically, this determination is unsure at best and often impossible.[21,35] In many cases it is hardly less difficult at autopsy. These problems have been stressed[13,14,41,61,71] and include the limitation of dissection at autopsy, the fact that often the embolus leaves no evidence of its origin and in many cases there is no way of determining whether or not a residual thrombus is in reality the point of origin of the embolus. The extensiveness of the thrombosis found at autopsy may prohibit the determination of its point of origin. The predominance of left sided thromboses[18,34,48,59] is considered by

some authors to be due to stasis caused by the pressure of the iliac artery on the left common iliac vein and has given rise to the belief by some that the thrombosis may begin at this point of compression and extend distally. In a similar manner it is possible for thrombi to form retrograde both into and from the veins of the pelvis. The belief that this retrograde formation does occur is well founded.[8,23,33,43]

Thrombi extending into both pelvic and femoral veins have been found at autopsy and it is at times impossible to determine its point of origin.

The controversy as to the frequency with which pelvic veins give rise to pulmonary emboli is reflected by the following opinions found in the literature. The divergence of opinion reflects the change in concept of origin of pulmonary embolism. In 1920 Hampton and Wharton[36] indicate that the pelvis is the usual source, with about 15 per cent arising from the legs. In 1928 Hall[33] quotes other authors as stating that 85 per cent arose from pelvic veins. Belt[12] in 1939 states, "The origin of the emboli is usually found in the thrombosed veins of the thigh or pelvis." Bauer[10] in 1941 states that ". . . almost without exception the thrombotic process has its origin in the deep venous trunks of the lower extremity." Allen[4] in 1943 indicates that embolus practically never arises from pelvic veins. In 1945 Allen[3] quotes Castleman in a personal communication as estimating that 95 per cent arise from the deep veins. Bauer[11] in 1946 states, "My own investigations have led me to conclude that it (thromboembolism) almost always arises in the deep veins of the lower leg and only in about 3 per cent of cases in the thigh or pelvis." Ochsner[58] in 1949 states that phlebothrombosis ". . . occurs almost without exception in the veins of the lower extremity. . . ." However, McPheeters[49] in 1945 states, "I believe there is a phlebothrombosis of the pelvic and hypogastric veins far more often than we think," and Bancroft[8] in 1949 indicates that pelvic thrombosis following pelvic procedures gives rise to pulmonary embolus not infrequently.

Although it is acknowledged that it is difficult and possibly misleading to interpret the statistics of others, particularly in view of the possible sources of error in examination of necropsy material which have been discussed above, the statistics in the literature indicate a fairly large number of thrombi were found to arise in pelvic veins. The published data on various series of thromboses, with and without pulmonary embolism, has been reviewed.[6,7,12,13,14,18,19,22,30,32,34,36,37,40,41,42,43,46,47,48,52,54,59,61,63,71,76]

Those in which an evaluation could be made showed an incidence of pelvic thromboses ranging from approximately 5 per cent to a conservative estimate of 40 per cent, the majority in the neighbor-

hood of 10 to 15 per cent. These reports included several series of fatal pulmonary embolus.

The following original series of a study of the incidence of pulmonary embolism at autopsy is presented which shows a relatively high incidence of pelvic thrombosis associated with fatal pulmonary embolism. It is concerned only with the type of embolus composed of blood elements, *i.e.*, neoplastic, fat and bacterial emboli are not included. It is to be noted that many of the difficulties in the evaluation of autopsy material which were mentioned above apply to this series, including the inability to completely dissect the veins of the extremities in every case.

This study covers a 13 year period including records of 1,723 consecutive autopsies taken from the files of the Department of Pathology, Medical College of Georgia, and available corresponding clinical records from the University Hospital on all cases in the study. This series of 1,723 consecutive autopsies included 454 cases of patients of 12 years or less in which no incidence of pulmonary embolism was encountered. There were, in this series of autopsies, 126 cases of pulmonary embolism.

These cases were grouped according to effect; *i.e.*, whether or not the embolism was fatal. The difficulty in ascertaining the effect of the embolism is admittedly great as has been noted.[26,27,31,54,62] However, only those emboli which were massive enough to cause death per se were included in the group of fatal emboli, so that the classification is considered to be reasonably accurate. In the group of fatal emboli there were a total of 37 cases.

Examination of the total series of 126 cases of emboli reveals that it is consistent with other published data of this nature as regards sex, age and seasonal variation. There was a high incidence of heart disease and of emboli arising from cardiac mural thromboses in the nonfatal group. Also a higher number of cases of pelvic thrombophlebitis was found in the nonfatal group, although the percentage of pelvic thrombosis was considerably lower in the total group than in the group of fatal emboli alone.

The group of 37 fatal emboli was studied in some detail. The thrombi found in these cases were in the following location: 1. Four arising in the hypogastric vein, two of these extending into the vena cava. 2. Three occupying the common iliac, apparently arising from the pelvic veins. 3. Three in the external iliac vein. 4. Five in the femoral vein, one extending into the iliac vein, one extending into the vena cava. 5. Fourteen in which no thrombi were found, nine of these almost certainly arising from veins of extremity (on the basis of clinical and autopsy data) and five probably arising from the

lower extremity. 6. In 8 cases mural cardiac thrombi were found which may or may not have been the source of the embolus. Quite likely a part or perhaps all of these arose from the lower extremity.

We see, therefore, in this series of 37 fatal emboli that the source of the embolus was apparently from the pelvic veins in 7 cases, or in 18.9 per cent of the cases, which is somewhat higher than that generally reported.

The high incidence of pelvic thromboses as a source of fatal pulmonary embolism in this series leads to speculation as to the cause. Study of both the fatal and nonfatal group shows a higher percentage of females in the group of fatal cases. The average age is appreciably lower in the fatal than the nonfatal. The incidence of pelvic operations and pelvic pathology is very high in the fatal group. This would seem to indicate that fatal pulmonary emboli may arise not infrequently from pelvic veins in younger females where pelvic operations and pathology are more prone to occur.

Whether this is correct or not, this study indicates the need for a greater recognition of the pelvic veins as a possible source of pulmonary embolism.

Summary

1. A study has been made of the literature to determine the frequency of pelvic thrombosis as a source of pulmonary embolism, and its clinical significance considered.

2. A series of cases of pulmonary embolism found at autopsy with a relatively high incidence of pelvic thrombosis is presented.

3. A proper recognition of the pelvic veins as a possible source of pulmonary embolism is advocated.

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CARCINOMA OF CERVIX UTERI

A Simple and Adequate Method for Detection Applicable to Office Practice

JOSEPH M. ECHOLS, M.D.*
GUY L. CALK, M.D.**
WILLIAM S. BOYD, M.D.***
Augusta

IT IS generally, but not universally conceded, that carcinomas may occur without disturbance of relations. A preinvasive phase frequently precedes the invasive stage of carcinoma of the cervix uteri.[1-11] Carcinoma of the cervix in its preinvasive stage can be cured, therefore pathologic recognition assumes considerable importance. Novak[12] has observed that preinvasive carcinoma may be present in a normal appearing cervix. Pund et al[3,13] have demonstrated that advanced invasive may be present in a clinically innocent cervix, and conclude that invasion frequently remains within the endocervical canal for a period of time before penetration of the portio vaginalis occurs.

The study of exfoliated cells, which was initiated by Papanicolaou and Traut[14] has become well established as a valuable aid in the detection of cervical carcinoma; however, histological confirmation is necessary before therapy is instituted.

Biopsy of the cervix has been a common procedure for many years, but, as pointed out by Foote and Stewart,[15] biopsy alone may frequently fail to detect a preinvasive carcinoma. Furthermore, Novak,[12] Pund[1,13,16] and Galvin and TeLinde[17] have reported that biopsy alone will frequently fail to differentiate a preinvasive from an invasive carcinoma. For these reasons we have strongly recommended multiple cervical biopsies and thorough endocervical curettage.[13,16] Meyer,[18] Schiller,[2] Knight,[7] and Younge[8] have also mentioned the value of endocervical curettage. In a previous paper,[16] a series of 71 cases of preinvasive carcinoma of the cervix was reported in which the diagnosis in 25 depended upon the examination of the endocervical scrapings.

Multiple biopsy and thorough endocervical curettage constitute an adequate diagnostic survey of the cervix, and not until those procedures are performed can the physician be certain that carcinoma

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From the Department of Obstetrics and Gynecology, Medical College of Georgia.
*Assistant Resident, Obstetrics and Gynecology.
**Resident, Obstetrics and Gynecology.
***Assistant Professor of Clinical Obstetrics and Gynecology.

of the cervix is ruled out. It would be impractical to hospitalize every patient with a suspicious cervix for diagnostic curettage and biopsy under general anesthesia. A diagnostic survey which is adequate and which may be performed as an office procedure requiring only a minimal amount of time and effort on the part of the physician, and within the economic grasp of every patient is much to be desired. A method of diagnostic survey is presented in the following paragraphs with a summary of the results obtained.

In July 1949 a diagnostic clinic was established in the outpatient department of the University Hospital, to which patients who were suspected of having carcinoma either because of clinical aberrations or because of positive cytology, were referred. The patients were subjected to multiple cervical biopsies, endocervical curettage and when feasible endometrial suction biopsy.

Method. After thorough cleansing of the perineal region and vagina with aqueous zephiran solution, biopsies by means of punch are taken from the junctional endocervix at six different points. Using a small serrated uterine curette, the endocervical canal is scraped in its entirety. In some cases endometrial suction biopsy is secured from the anterior and posterior endometrial surfaces.

As a general rule, no analgesic agents are necessary because very little pain is associated with curettage in the absence of instrumental dilatation of the cervix. If the patient is apprehensive and is likely to have a low pain threshold, intravenous Demarol is an aid. For a comparatively painless procedure, paracervical injection of a local anesthetic agent may be utilized.

Thorough electrocauterization of the cervix is done as a matter of routine following the diagnostic survey. Bleeding following multiple biopsy of the cervix has not been a problem. An occasional patient will exhibit unusual bleeding tendencies, particularly those with increased vascularity due to pregnancy, but this is adequately controlled in the majority of cases by electrocoagulation and by placing a tampon adjacent to the cervix in the upper vaginal vault.

Infection has been totally absent even without the use of prophylactic antibiotics and chemotherapy.

Results. One hundred and thirty-three patients have been surveyed in the diagnostic clinic or private office. Only 42 of these patients had endometrial suction biopsy. The ages of all patients ranged from 18 to 72 years with an average age of 37.79 years. Borderline changes were found in 9 (6.76 per cent) with an average age of 29.3 years. Preinvasive carcinoma was diagnosed in 24 cases (18.04 per cent) with an average age of 34.5 years. Invasive carcinoma was found in 8 cases (6.01 per cent) with an average

age of 40.8 years. Specimens of the cervix obtained from one patient, 26 years of age, contained typical tubercles in which acid fast bacilli were demonstrated. Of the 42 cases from which endometrial suction biopsy was secured, one far advanced adenocarcinoma of the endometrium was found (table I).

Twenty-eight of the 32 cases with carcinoma of the cervix had cytological studies prior to any diagnostic procedure. Twenty-seven of these had either suspicious or positive exfoliated cellular spreads. In one case of preinvasive carcinoma of the cervix the cytological examination was reported negative. Five of the 9 patients with borderline changes had cytological studies, all of which were either suspicious or positive. The one case with far advanced adenocarcinoma of the endometrium had negative cervical and vaginal cytology. There were 22 instances of suspicious or positive cervical spreads in which no malignancy or borderline changes were demonstrable by diagnostic survey (table 2).

Fifteen cases diagnosed as preinvasive carcinoma of the cervix had further surgical therapy following the diagnostic survey. Eleven had total abdominal hysterectomy, 2 had surgical conization of the cervix, one cervical stump was excised, and in one case dilatation and curettage were performed under general anesthesia. Remains of preinvasive carcinoma were found in 13 while no remains could be found in two of the specimens submitted following the additional surgery. In no instance was invasive carcinoma present in which a diagnosis of preinvasive carcinoma had been established prior to the additional surgery.

Discussion

The incidence of preinvasive carcinoma of the cervix has been reported at 3.9 per cent in the clinically innocent cervix by Pund and Auerbach[19] and 1.15 per cent in the abdominal cervix by Younge, Hertig and Armstrong.[8] The average incidence of invasive carcinoma of the cervix is 1.6 per cent as reported by Meigs.[20]

The average age of preinvasive carcinoma of the cervix has been reported at 36.6 years by Pund and Auerbach,[19] 37.1 years by Galvin and TeLinde,[17] and 38.7 years by Younge et al.[8] The 24 cases of preinvasive carcinoma herein reported show an average age of 34.5 years. As previously indicated, 8 of our cases had invasive carcinoma with an average age of 40.8 years, in contrast to the generally accepted average age of 48 years.[17,19]

The above differences indicate the value of an adequate diagnostic survey and prove the efficiency of the method advocated.

Two cases which were diagnosed as preinvasive carcinoma con-

TABLE I

Results of Diagnostic Survey

	Borderline Changes	Preinvasive Carcinoma	Invasive Carcinoma	Tuberculosis of Cervix	Adenocarcinoma of Endometrium	Negative for Cancer	All Cases
Cases	9	24	8	1	1 of 42	101	133
Per Cent	6.76	18.04	6.01	0.7	...	75.95	100
Average Age	29.3	34.5	40.8	26	72	...	37.79

TABLE II

Results of Cytological Studies

Papanicolaou Smears	Cases without Carcinoma	Cases with Carcinoma of Cervix	Cases with Borderline Changes	Adenocarcinoma of Endometrium
Suspicious	9	3	2	0
Positive	13	24	3	0
Negative	...	1	0	1

TABLE III

Further Studies on Cases with Diagnosis of Preinvasive Carcinoma

	Repeat Office Curettage	Hysterectomy	Dilatation and Curettage	Excision of Cervical Stump	Surgical Conization of Cervix
Remains of Preinvasive Carcinoma Present	0	10	0	1	2
No Remains of Preinvasive Carcinoma Present	2	1	1	0	0
Invasive Carcinoma Present	0	0	0	0	0

comitant with intrauterine pregnancy were encountered. These patients were carefully observed throughout their prenatal course and allowed to deliver vaginally at term. Repeat diagnostic surveys have revealed no evidence of carcinoma six months postnatally in one and one month and five months postnatally in the other. The significance of preinvasive carcinoma of the cervix during pregnancy remains a problem to which considerable attention at present is being given. Two case reports of preinvasive carcinoma of the cervix concomitant with pregnancy which we have had an opportunity to observe follow:

CASE 1. Mrs. M. G., 23 year old white gravida 4, para 4, was first seen Dec. 30, 1949, complaining of pain in the right lower quadrant and menstrual irregularity. Examination revealed the uterus to be enlarged to the size of a three months' pregnancy. Routine vaginal and cervical exfoliated cellular spreads were made. The cytological report was Grade IV malignant cells. On Jan. 24, 1950, endocervical curettage, biopsy and cauterization of the cervix was performed in the diagnostic clinic. The specimens revealed squamous cell carcinoma confined to the natural surfaces in one of six sections from the cervix. Vaginal and cervical cellular spreads were repeated on April 1 and May 12, 1950, and both were reported as having small number of cancer cells present. This patient had a spontaneous vaginal delivery on June 13. Following delivery and discharge from the hospital the patient was instructed to return to the diagnostic clinic in six weeks, but was not seen again until Jan. 9, 1951, at which time a survey consisting of endocervical curettage, multiple biopsies of cervix, endometrial suction biopsy, and electrocauterization of the cervix was performed in the outpatient department. The pathological examination of the specimens revealed chronic inflammation of the cervix with foci of squamous metaplasia but no remains of the carcinoma could be seen in the five sections of cervix. This patient is to be surveyed at intervals of six months in the future.

CASE 2. Mrs. V. G., 24 year old white gravida 5, para 3, abortus 1, was seen in the gynecological clinic on Mar. 27, 1950, complaining of heaviness in her pelvis. Pelvic examination revealed moderate relaxation of anterior vaginal wall and perineum with slight decensus of the uterus. Routine vaginal and cervical exfoliated cellular spreads were made, the study of which revealed marked nuclear changes. The patient was referred to the diagnostic clinic on April 18, at which time endocervical curettage, endometrial suction biopsy, multiple biopsies of cervix, and electrocauterization were performed. A pathological report of squamous cell carcinoma limited to the natural surfaces in four of the six sections of junctional endocervix was obtained. This patient was admitted to the hospital on May 10 for total abdominal hysterectomy but related that her last regular menstrual period was April 5. She was anxious to have another child and in view of the possibility of a pregnancy, it was decided to follow this patient carefully in the outpatient department. Vaginal and cervical cellular spreads were made at monthly intervals during the prenatal course. The reported findings ranged from slight nuclear changes to Grade IV malignant cells. On Jan. 3, 1951, this patient had a spontaneous vaginal delivery and upon discharge from the hospital was instructed to return to the diagnostic clinic on January 30. On return of the patient at this time endocervical curettage, endometrial suction biopsy and multiple biopsies with elec-

trocauterization of the cervix were performed. Pathological examination revealed chronic inflammation in the five sections of cervix. The endocervical scrapings showed a similar result. On May 1, 1951, this patient returned to the diagnostic clinic and the survey was repeated. Again pathological examination revealed chronic inflammation in the sections from the cervix. It is of interest to wonder what the role of electrocauterization may have played in controlling the findings which was observed in this patient's cervix. Diagnostic surveys will be performed at six month intervals in the future.

Note: We wish to express our appreciation to Dr. E. R. Pund, Professor of Pathology, for his interest in the pathological examinations of the specimens and encouragement in establishment of the diagnostic clinic.

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ANTICOAGULANTS IN OBSTETRICS, WITH A CASE REPORT

C. W. Coolidge, M.D.*
Richard Torpin, M.D.**
Augusta

Thrombophlebitis and phlebothrombosis with their embolic sequelae are becoming a more prominent cause of maternal mortality as attested by the change in mortality rates in the past 25 years. This may be explained by improved prenatal care, the use of antibiotics and better facilities to cope with hemorrhage. Since figures in various localities differ, it may be assumed that between 7 to 12 per cent of maternal deaths are due to embolic phenomena.[1,2,3,4,24] The use of anticoagulants in the prevention of embolism by lowering the coagulability of blood is a more or less direct approach to the problem. The anticoagulant drugs have also been credited with shortening the hospital stay and reducing the future discomfort in patients with these conditions.[5,6]

Heparin and dicumarol have been exhaustively investigated and the literature on their use is voluminous. Because of the low cost and the effectiveness when administered orally, dicumarol is the drug most frequently used. In the lag period of 36 to 72 hours prior to dicumarol effectiveness, heparin is usually used. Heparin, though as effective as dicumarol, is considerably more expensive and must be administered by continuous intravenous infusion, intermittent intravenous injection or intramuscular injection of repository preparation. The intramuscular route is not without considerable discomfort to the patient.

All important in the administration of these agents is the mensuration of their effect by accurately performed laboratory tests and careful clinical observation. This point cannot be overemphasized when using dicumarol as 1 patient in 5 will show an exaggerated response to the drug and is thereby exposed to the everpresent danger of hemorrhage. When heparin is used the dose should be sufficient to double or triple the clotting time. This dose varies between 300 and 400 mg. daily.[7] For the average patient 14 mg. per hour must be available and the entire effect of the average therapeutic intravenous dose expires in less than four hours. With dicumarol Moss et al[8] showed experimentally that there was no suppression of thrombus formation until prothrombin time is less

From the Department of Obstetrics and Gynecology, Medical College of Georgia.
*Assistant Resident, Obstetrics and Gynecology.
**Professor of Obstetrics and Gynecology.

than 40 per cent of normal. The maintenance of prothrombin activity at 10 to 30 per cent of normal is usually recommended because thrombus suppression is at a maximum at these levels and the greatest incidence of hemorrhage occurs when prothrombin activity is below 10 per cent of normal. This is secured by the administration of a 300 mg. initial dose. Prothrombin time is determined at this time and daily thereafter. The second daily dose is usually 200 mg. but it and subsequent doses are decided only after considering the results of prothrombin determinations.[9,10,11,12]

The application of this therapy to the obstetrical patient inspires even more caution than in medical or surgical patients. Kraus et al[13] showed in rabbits that near therapeutic levels there was no adverse effects on the fetus. In the same experiments they showed that when unsafe prothrombin levels were reached (below 10 per cent) that no mothers survived delivery and all fetuses died a hemorrhagic death in utero. Quick[14] has reported that prothrombin activity in newborn dogs is depressed to a greater degree than in the mother. Adamson, Weaver and Jaimet[15] report no fetal complications in their patients who received dicumarol prior to delivery. Bauer[17] who uses heparin alone had no complication in obstetrical patients in his series. However, Sachs and Labate[18] have reported a case near term in which intrauterine fetal death from hemorrhage occurred on the fifty-third day of dicumarol treatment. In this case there were no hemorrhagic complications in the mother.

When delivery is imminent, the preponderant opinion in the literature is that dicumarol should be discontinued, and Vitamin K and possibly freshly drawn blood should be administered to return prothrombin activity to normal, as is done in patients undergoing surgery.[12,13] However, Jaimet[16] reports in his series 3 cases of cesarean section and 2 patients who had placentas removed manually while receiving dicumarol. In thrombo-embolic disease he recommends that the patient be immediately dicumarolized and prothrombin time be maintained at 34 to 40 seconds at the time of delivery. There were no hemorrhagic complications in his cases.

The anticoagulants have been used extensively in the puerperal period and most authors are of the opinion that they cause no increase in postpartum bleeding.[6,10,15,16,17] This opinion is supported by Barnes and Ervin[19] who in a controlled series measured the actual hemoglobin loss in patients receiving dicumarol. Though there was no significant increase in blood loss in the dicumarol treated patients it is of interest to note that 2 of 5 patients who received heparin and dicumarol developed hematomas at the episiotomy site and one experienced a partial breakdown. The prothrombin activity of

these patients was never below 33 per cent of normal and clotting time was never more than two and one-half times normal.

Concerning perineal hemorrhagic complications Smith and Mulligan[20] administered dicumarol prophylactically to 2,353 postoperative cases. Vaginal bleeding of a significant degree occurred in a ratio of 1 in 117 cases. Though the same incidence was found in untreated cases of earlier period, in a later series prothrombin activity was not allowed to fall below 40 per cent of normal and the incidence of vaginal bleeding was more than halved.

Brambel and Hunter[21] have shown that when prothrombin activity is maintained at 40 to 50 per cent of normal there is no depression of prothrombin activity in the nursing infant. Field[22] showed that at lower maternal prothrombin levels the response of the suckling offspring is out of proportion to that of the mother. This latter work inspires a degree of caution and leads one to believe that the nursing infant should be afforded the protection of frequent prothrombin determinations and the administration of Vitamin K when indicated.

Of the newer anticoagulants, tromexan, though not extensively investigated, seems to offer a greater ease of control than dicumarol in that it is effective in 24 to 36 hours in 80 per cent of patients. Its cost is considerably greater than dicumarol and its dosage is approximately four times greater which is disadvantageous. Prothrombin time is a measure of the effect of the previous days' dosage rather than the effect of the dose administered 48 to 72 hours previously with dicumarol. Return to normal prothrombin levels occurs in 24 to 36 hours after the drug has been discontinued in most cases.[23]

The following is a case which developed a hematoma of the vulva during heparin and dicumarol therapy for thrombophlebitis in the immediate postpartum period:

A. M. L., a 21 year old Negro primigravida, was admitted the evening of February 8. She had received no prenatal care and was uncertain as to her last menstrual period though she thought it to be mid May. She denied symptoms of toxemia other than pedal edema during the last month of gestation. Her membranes had ruptured the morning before admission and irregular contractions began shortly thereafter.

Physical examination revealed a Negro female of median constitution type having uterine contractions of poor intensity at 5 minute intervals. Temperature was 98.8, pulse 110, respirations 22 and blood pressure 140/100. The abdomen was distended with an intrauterine pregnancy and the fundus measured 29 cm. Rectal examination showed no cervical dilatation. There was bilateral trace of pretibial edema. Physical examination was otherwise negative.

Laboratory examination on admission showed hemoglobin 10.5 Gm. Urinalysis revealed 2 plus albumin and an occasional white blood cell. X-ray

pelvimetry showed a pelvic inlet 10.3 by 10.1 cm. with a midpelvis of 10 cm. The biparietal diameter of the fetal head was 8.5 cm.

During the first 24 hours of hospitalization uterine contractions were of poor quality and little progress was made. In addition to a liquid diet she received 2,000 cc. 5 per cent glucose in distilled water and four intravenous injections of 1 Gm. of magnesium sulphate. The evening following admission she was given ¼ grain of morphine and slept until 1:30 a.m., when normal labor began. Shortly thereafter it was found that a positive Homan's sign was present on the left and there was tenderness of the left calf and over the left femoral veins. There was a 2 plus edema of the left leg and no edema of the right leg. Temperature was now 100.2 with a pulse of 112 and blood pressure 130/88.

Antibiotic therapy was started but as delivery seemed imminent no anticoagulant therapy was prescribed. The leg was elevated in full extension and hot moist dressings applied. A normal 6 pound 3 ounces male infant was delivered by midforceps operation at 1 p.m. the following day. The right mesiolateral episiotomy was repaired using a continuous suture of chromic catgut. Estimated blood loss was 200 cc. As decided in consultation with the medical service, anticoagulant therapy was started immediately after delivery. Heparin mg. 50 was given intravenously and 200 mg. of deporheparin was given intramuscularly. The intravenous heparin was repeated at 6 p.m. and at midnight. Dicumarol 300 mg. was given orally and 200 mg. was given the following morning.

During the first 24 hours postpartum, vaginal bleeding was enough to soak eight perineal pads and 500 cc. whole blood was administered. There was some swelling around the episiotomy site on the evening of the first postpartum day and an ice cap was applied to the perineum. There was no vaginal bleeding at this time.

The perineal swelling increased and extended to the right labium and over the right ischiorectal space. Prothrombin time the following morning was 27.4 sec., 100 per cent-16.3 sec., 30 per cent-23.1 sec. and 20 per cent-30.6 sec. Hemoglobin was 3.5 Gm. Blood pressure was 120/70 with pulse 110. One thousand cc. of whole blood and 72 mg. of vitamin K was given intravenously and the patient was taken to the operating room where the episiotomy repair was taken down. Four hundred and fifty cc. of clotted blood was removed and the wound was reclosed and the vagina was packed. No bleeding point was found. One thousand cc. of whole blood was given in surgery and an additional 500 cc. was given when the patient was returned to the ward. The perineum remained swollen.

The following morning prothrombin time was normal and additional transfusions were given on the next two days. On the fifth postpartum day the episiotomy opened and began to drain sanguineous, purulent material. At this time no evidence of thrombophlebitis was present. Antibiotics were supplemented by sitz baths on the tenth day and the wound began to heal. The patient was discharged on the twenty-second postpartum day. At no time were signs of pulmonary embolism present.

In conclusion, it may be stated that though the anticoagulants are of use in prevention of emboli and in suppressing other postthrombotic sequelae their use is not without danger. The use of an accurately performed prothrombin time and clotting time determina-

tions as an adjunct to careful clinical observation is absolutely mandatory when heparin and dicumarol are used in obstetrical patients.

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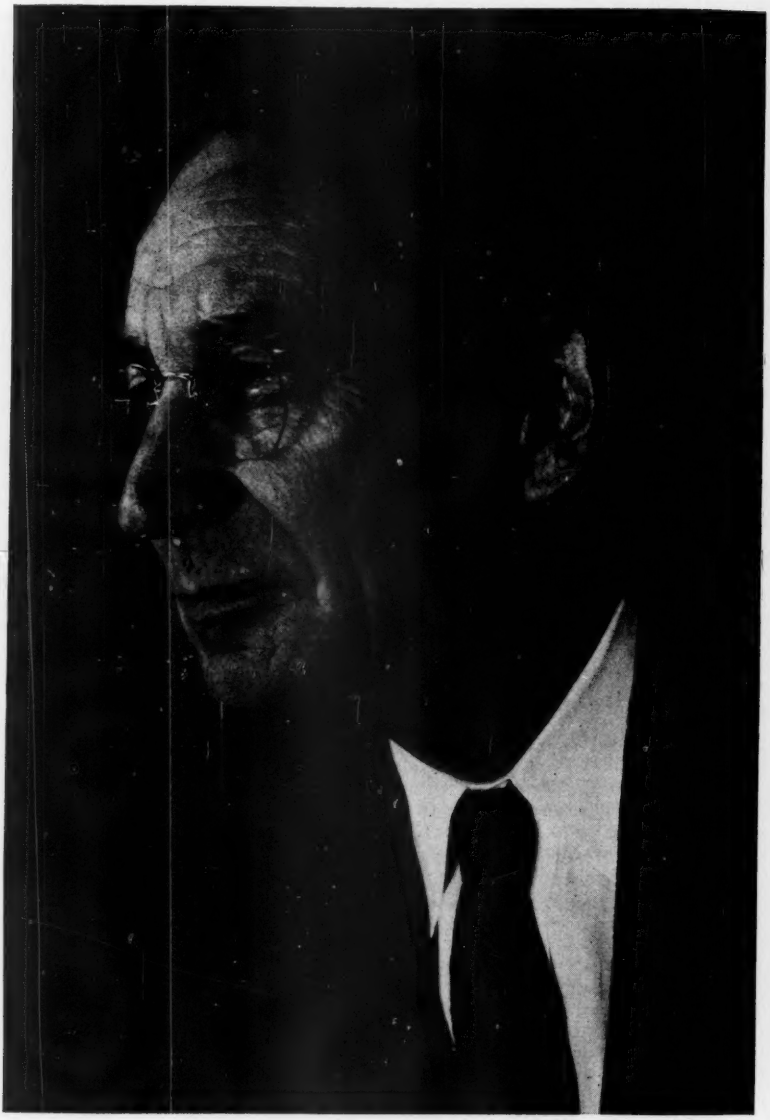

G. LOMBARD KELLY, M.D., *President*
The Medical College of Georgia

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THE MEDICAL COLLEGE OF GEORGIA NUMBER

The Medical College of Georgia was originally chartered in 1828 as the Medical Academy of Georgia. The following year the name of the institution was changed to the Medical Institute of the State of Georgia. In 1833, the name was changed to the Medical College of Georgia. In the intervening years the school has operated under two other names: from 1873 to 1933 the school was known as the Medical Department of the University of Georgia; from 1933 until January 1950, it was called the University of Georgia School of Medicine. In January 1950 the name, Medical College of Georgia, was restored. The Medical College of Georgia has operated continuously since its founding except for two years during the Civil War when classes were suspended.

The Medical College of Georgia was essentially a private school until 1873 when it became affiliated with the University of Georgia. Since Jan. 1, 1932, it has been one of the units of the University System of Georgia, and its administration since then has been responsible only to the Chancellor and Board of Regents. Funds for its support are now allocated by the Board of Regents; whereas,

until 1932 there was a separate Board of Trustees and a separate appropriation made for its support by the State Legislature.

From its beginning, the Medical College of Georgia has depended upon the city hospital and the out-patient department of the city of Augusta for clinical material. The old Medical College building erected in 1835 was abandoned for teaching purposes in 1914. The old City Hospital which was adjacent to it has been razed. In 1914 the present University Hospital was completed and the present Administration building was leased and remodeled for medical school purposes. In 1937 the Dugas building was erected and in 1939, the Murphey building. In 1940 the Medical College of Georgia expanded its admission of first-year students from 48 to 76, and since that time the number admitted has been increased to 82. A further increase in enrollment is planned on completion of the proposed new State general hospital.

Plans are now being drawn for a State general hospital of 768 beds to be erected on land adjacent to the Dugas and Murphey buildings, already in possession of the Board of Regents. Funds have been allocated by the Board for the construction of a new administration building at a cost of some $600,000. This building will probably be placed immediately adjacent to the Dugas and Murphey buildings, and the State hospital will very likely be placed immediately in front of the new Administration building site. The cost of the State general hospital, equipped, will be approximately $10,000,000. The Legislature at its most recent session provided a total of $12,000,000 for this purpose in case that much is needed. There will be separate quarters constructed for the resident staff members and a separate building for student nurses. Fortunately there is ample space for all these buildings.

In the new State general hospital there will be 100 beds provided for teaching and research in cancer, 50 beds for psychiatry and 50 beds for tuberculosis. The remaining beds will be for general medicine and surgery cases.

The out-patient department of the University Hospital will be employed for teaching purposes, and the domiciliary medicine will continue as it has for the past quarter of a century with senior students attending patients in their homes under supervision. The present University Hospital will be depended upon for the teaching of Obstetrics as it is not planned to bring normal obstetrical cases into the State hospital. The present model Maternity Shelter in the Administration building will be continued and enlarged.

Eventually it is planned to acquire adjacent properties and to complete an outstanding Medical Center. When the State general

hospital is in operation, it will be possible to carry out the plan to integrate medical education and medical care in Georgia by a rotation system of resident staff members and teachers throughout the various State hospitals. It is hoped also that assistance will be given to smaller hospitals throughout the State and that more of the graduates will find it possible to obtain postgraduate training in the State. This will mean that fewer of the graduates of the school will locate outside the State to practice.

We have watched with pride the growth and improvement of our sister medical schools in the South, and we join with them in the ambition to carry on the traditions of Medicine exemplified by such eminent physicians as Marion Sims, Crawford W. Long, and others. We deeply appreciate the honor of having been invited to sponsor a special number of THE AMERICAN SURGEON.

G. LOMBARD KELLY, M.D.
President and Professor of Anatomy
The Medical College of Georgia
Augusta, Ga.

The Sixteenth Annual Assembly of the United States Chapter
International College of Surgeons
will be held at the Palmer House in Chicago
September 10-13, 1951

For details, write DR. ARNOLD S. JACKSON, *Secretary*
United States Chapter, International College of Surgeons
1516 Lake Shore Drive, Chicago 10, Illinois

SECTIONAL MEETING OF THE SOUTHEASTERN SURGICAL CONGRESS

Maryland will be the host this year for the conjoint sectional meetings of the Maryland, Virginia, District of Columbia, and West Virginia sections of The Southeastern Surgical Congress. The meeting is scheduled for Baltimore, Maryland, September 13-15, inclusive.

The four groups which met at White Sulphur Springs, W. Va., last year, plan to organize into the Northeast Section of The Southeastern Surgical Congress, and each year the meetings will alternate between the four states.

Dr. W. Raymond McKenzie, chairman of the Maryland section, is general chairman for this year's meeting, while Dr. George H. Brouillet, also of Baltimore, is chairman of the program committee.

This year's meeting will be marked by operative clinics at two Baltimore hospitals on Thursday and Friday mornings, with scientific programs in the afternoons and on Saturday morning. Members of the Congress are invited to attend the meeting, and programs may be obtained by contacting Mr. R. J. Wilkinson, Jr., secretary of the West Virginia section, at 1119 Sixth Avenue, Huntington, West Virginia.

The executive committee of the Northeast Section will be composed of the chairmen of the four state groups and Mr. Wilkinson. Headquarters for this year's meeting will be the Lord Baltimore Hotel.